# "DOSIMETRIC COMPARISON OF 3D TREATMENT PLANNING AND CONVENTIONAL PLANNING IN POST-OPERATIVE VAGINAL MOULD BRACHYTHERAPY (VBT) FOR PATIENTS WITH GYNECOLOGICAL MALIGNANCIES"

**DEPARTMENT OF RADIATION ONCOLOGY,**
**CHRISTIAN MEDICAL COLLEGE,**
**VELLORE, TAMIL NADU 632004**

**DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF**

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**CHENNAI – 600032**


# Certificate

This is to certify that the dissertation entitled '**DOSIMETRIC COMPARISON OF 3D TREATMENT PLANNING AND CONVENTIONAL PLANNING IN POST-OPERATIVE VAGINAL MOULD BRACHYTHERAPY (VBT) FOR PATIENTS WITH GYNECOLOGICAL MALIGNANCIES**' is a bonafide work done by Dr. Jeyaanth P.V., Post Graduate Student in the Department of Radiation Oncology, Christian Medical College, Vellore during the period from April 2016 to April 2019 and is being submitted to The Tamil Nadu Dr. M. G. R. Medical University in partial fulfilment of the MD Branch Radiation Oncology examination conducted in May 2019.

Guide

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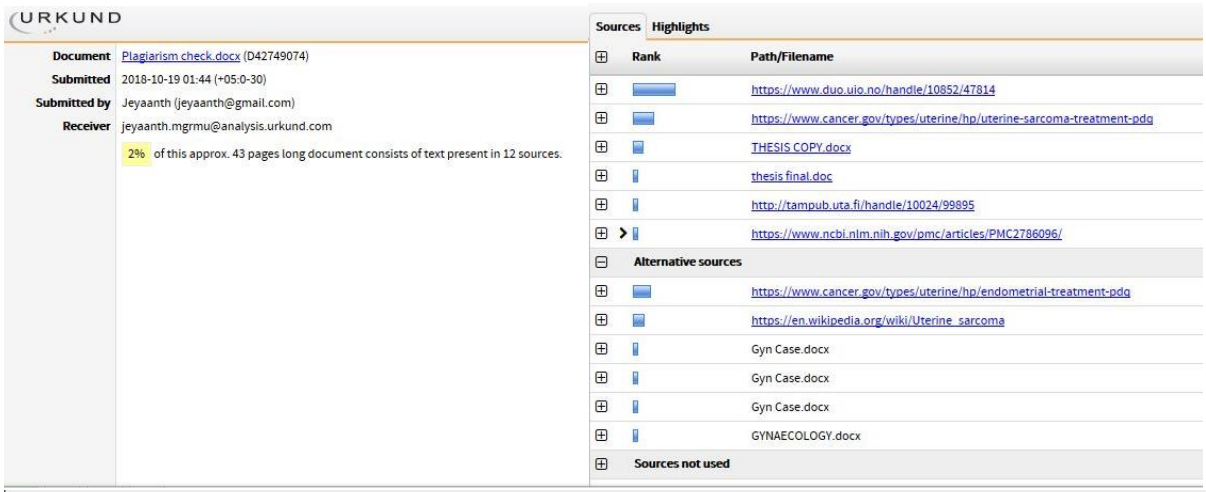

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## AIM

To dosimetrically compare 3D treatment planning and conventional planning in post-operative vaginal mould brachytherapy (VBT) for patients with gynaecological malignancies.

## OBJECTIVES

### Primary Objective

To compare dose to target and organs at risk in conventional planning Vs CT based 3D plan in vaginal mould brachytherapy

### Secondary Objectives

(1) To compare the effect of bladder distension on target dose distribution as well as dose to organs at risk.

(2) To assess the feasibility of CT based image guided vaginal brachytherapy (VBT) in gynecological malignancies

# LITERATURE REVIEW

## Introduction

Gynaecologic cancers comprise a group of cancers that originate in the female genital tract. The five major types of gynaecologic malignancies are cervical, ovarian, uterine (endometrial cancer and uterine sarcoma), vaginal and vulvar. The prevalence, incidence, and mortality rates for the gynecologic cancers vary across the globe. (1) Gynecological malignancies constitute a major cancer burden in Indian population and highest rate of cervical and endometrial malignancies in South Asia is seen among Indian women. (2)

## Cervical Cancer

Cervical cancers are relatively more common in India and is usually diagnosed late. In the past few years, due to improved screening programmes in India, carcinoma in situ and early invasive cervical cancer are detected at primary care level. Early invasive cervical cancers of FIGO stage 1A and 1B1 are primarily managed with radical surgery (Total abdominal hysterectomy + bilateral salphingo-oopherectomy +/- node dissection & Omental Sampling).

Patients with risk factors such as deep stromal invasion, lymphovascular invasion and size more than 4 cms were offered radiation therapy (External Beam radiation therapy followed by vaginal cuff brachytherapy).(1) Parametrial invasion, positive nodes and positive margins are considered as

high risk factors and these patients are offered concurrent chemotherapy in addition to radiation therapy.(2)

## *Endometrial Cancer*

Endometrial cancer is mostly diagnosed at an early stage. In-spite of low value for population screening, post-menopausal bleeding, menorrhagia and metrorrhagia leads to early detection of endometrial cancer. (3) Most women have favourable prognosis after treatment. although there are some histological high-risk features which warrants multimodality management. The primary modality of treating localized disease is radical surgery (Total abdominal hysterectomy + bilateral salphingo-oopherectomy +/- node dissection & Omental Sampling). Major prognostic factors for endometrial carcinoma are stage, age, histological type, grade, depth of myometrial invasion, and presence of lympho-vascular space invasion (LVSI). Adjuvant radiotherapy (RT) for endometrial carcinoma has increasingly been tailored to these risk factors. Based on prospective and retrospective data, endometrial carcinoma has been classified as low-risk, intermediate-risk, and high-risk for lymph node metastases and/or early disease spread to the abdominal cavity and to distant sites. The majority of patients with endometrial carcinoma have low to intermediate (55%) or high-intermediate (30%) risk features; only 15% have a high-risk profile (4). The results of the randomized trials for intermediate-risk endometrial carcinoma suggested that, in view of the absence of survival

benefit with external beam radiotherapy (EBRT) and of the fact that most (75%) locoregional recurrences were often seen in the vagina, vaginal brachytherapy (VBT) alone might be effective for patients with high-intermediate risk features to obtain local control with fewer side effects and better quality of life. (5)

## Vaginal Cuff Brachytherapy

Most of the data published lately on vaginal vault brachytherapy stem from 2D plain film-derived conventional plans. The most important drawback of this approach is that dose to adjuvant organs, mainly rectum and bladder may be inadequately assessed. With the advent of computed tomography (CT) based 3D planning systems, prescribed dose to the target volume and concomitant exposure to bladder, rectum and sigmoid colon can be clearly identified (6). However, the International Commission on Radiation Units and Measurements (ICRU) defines only bladder and rectal reference points in 2D plans which may not represent actual 3D dose distribution. Even more worrisome is the fact that doses to small bowel and sigmoid colon are simply ignored in conventional vaginal brachytherapy plans. In post hysterectomy status, small bowel loops and sigmoid colon tend to migrate to the pelvis and lie in close proximity to the vaginal vault and are at a risk of exposure to high doses of radiation. (7)

Most common vaginal mould application is with a single line source vaginal cylinder. The largest cylinder that can be comfortably accommodated in the vagina is placed to optimize the dose distribution and allow for apposition of the vaginal mucosa to the cylinder (8). In treating the vaginal vault, the treatment is complicated by proximity to normal tissues such as anterior rectal wall, the bladder base, sigmoid colon and small bowel. In recent surveys by American Brachytherapy society on practice patterns of American radiation oncology centers, most centers do not record the dose to OARs adequately (9,10).

Hence in view of paucity of data, this study was undertaken to assess and compare a conventional plan to a customized volumetric plan and analyse if there was advantage in terms of dose to the tumour and organs at risk.

## Epidemiology

### *Cervical cancer*

Globally, Cervical cancer is the fourth most common cancer in women. A large majority (around 85%) of the global burden occurs in the less developed regions, where it accounts for almost 12% of all female cancers.(3) There were an estimated 266,000 deaths from cervical cancer worldwide in 2012, accounting for 7.5% of all female cancer deaths. Almost nine out of ten (87%) cervical cancer deaths occur in the less

developed regions, hence mortality due to cervical cancer is also an indicator of health inequities. (3)

In India, every year 122,844 women are diagnosed with cervical cancer and 67,477 die from the disease. India has a population of 432 million women aged 15 years and older who are at risk of developing cancer. It is the second most common cancer in women aged 15–44 years. India also has the highest age standardized incidence of cervical cancer in South Asia at 22, compared to 19.2 in Bangladesh, 13 in Sri Lanka, and 2.8 in Iran. (4) In India, the peak age for cervical cancer incidence is 55–59 years. Current data from the National Cancer Registry Program (NCRP) indicates that the most common sites of cancer among women are the breasts and the cervix.(5) The recent NCRP data show that between 2009 and 2011 Aizawl district in the north eastern part of India had the highest levels of cervical cancer at an age-adjusted rate of 24.3, followed by Barshi at 19.5 and Bangalore at 18.9.(5) According to ICMR hospital based cancer registry report, cancer of the breast (24.3%) was the leading site followed by cervix (22.5%) in Chennai.(6) In women aged 30–69 years, cervical cancer was the leading fatal cancer in both rural and urban areas, with higher rates in rural areas. The age-standardised rates for

cervical cancer in women in Jammu and Kashmir and Assam were less than a quarter of the national rates for cervical cancer. (7)

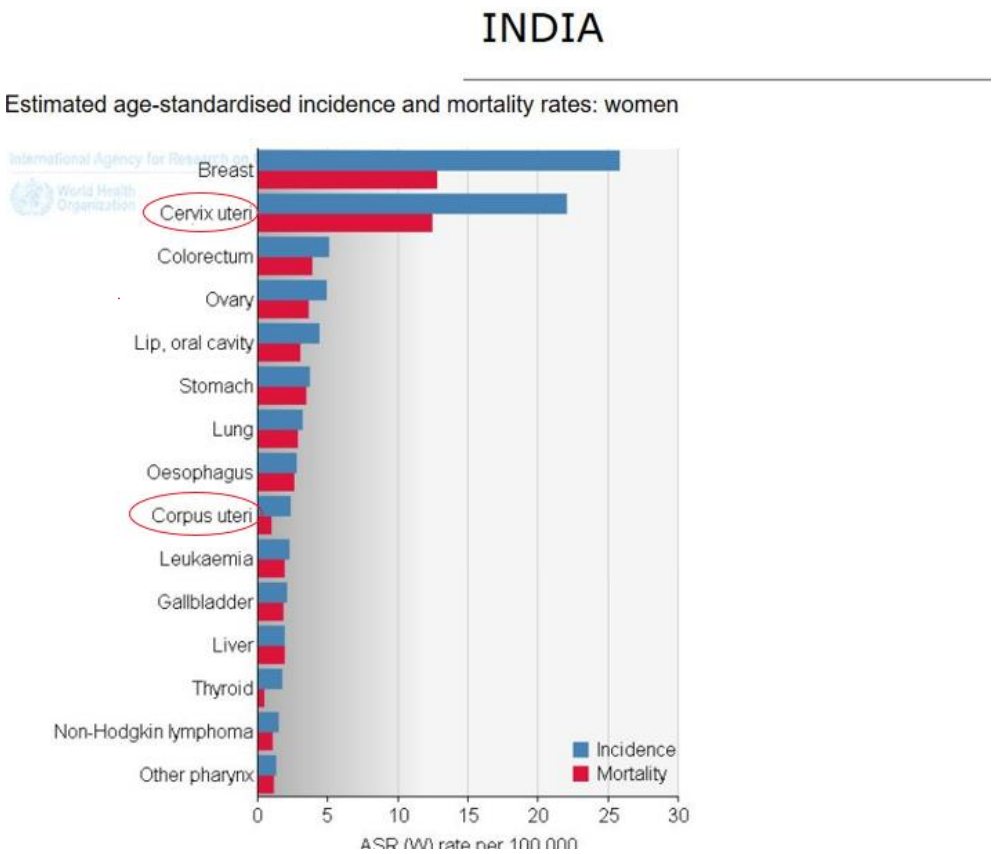



Fig 1: Estimated incidence, mortality and 5 year prevalence: Women, INDIA

Globocan 2012 (IARC)

## *Endometrial cancer*

Globally, cancer of the uterine corpus is one of five most common malignancies worldwide. Endometrial cancer is the most common gynaecological malignancy in developed countries.(3) According to 2017 Cancer Statistics data, incidence of endometrial cancer is on a rise in the United States of America strongly associated with obesity. Not only an increase in incidence rates were noted but also death rates rose from 2010

to 2014 by about 2 percent per year for uterine cancer. In survival analysis data published by the report, it was evident that the 5-year survival rate of localised early endometrial cancer was 95 percent with appropriate oncological management. Approximately 2.7 percent of women will be diagnosed with endometrial cancer at some point during their lifetime, based on SEER data.(8)

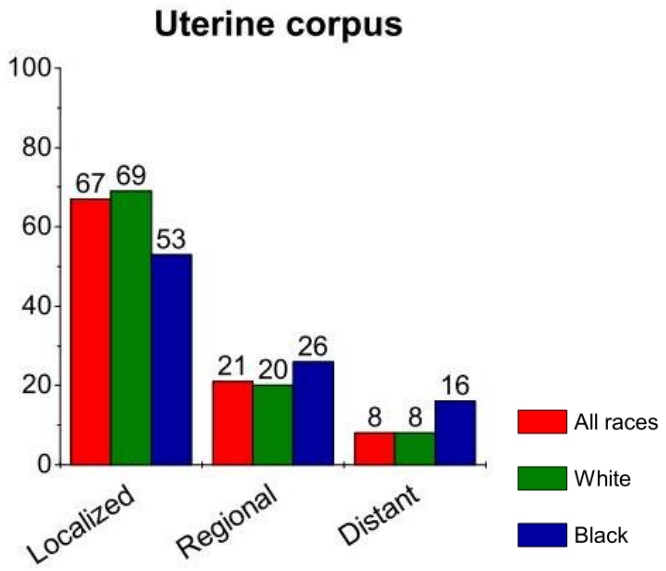



Fig 2: Stage Distribution by Race, United States, 2006 to 2012(8)

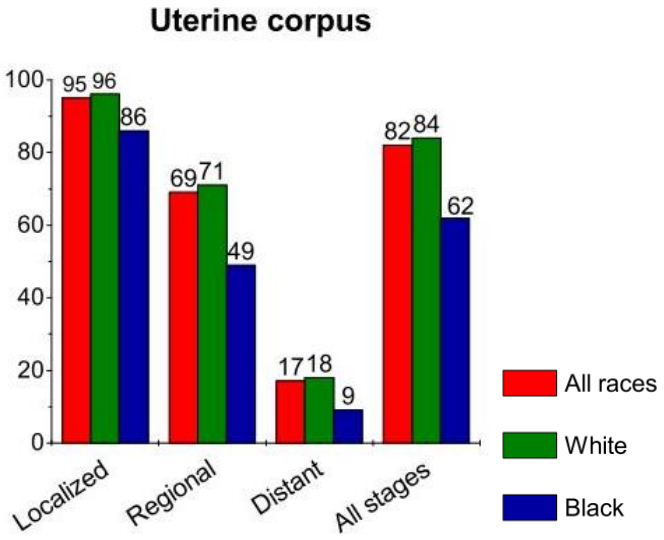



Fig 3: Five-Year Relative Survival Rates by Stage at Diagnosis and Race, United States(8)

In India, as opposed to global data, incidence and mortality of cancers of uterine corpus is relatively low. It comprises about 2% of all cancers in women in India. The incidence of endometrial cancer cases are very low in India; the highest being observed in Bangalore (ASR=4.2) and in Delhi (ASR=4.3), while in Mumbai it was 2.8 per 100,000.(6,9) Overall morbidity and mortality of endometrial cancer is low because most patients are postmenopausal and present at early stage because of abnormal bleeding, but it is associated with an approximately four fold increase in mortality with ovarian cancer and two fold increase in mortality with breast cancer (10) About 12,335 cases are diagnosed every year and 2773 cases die of this malignancy.(11) The declining incidence

of cervical cancer and the predicted rise of endometrial cancer in this century mean that endometrial cancer will be a significant issue in India.(12) Of the women diagnosed with endometrial cancer more than 75 percent are postmenopausal, only 3-10 percent are less than 40 years. But recent data showed increased incidence in younger age group due to increasing exposure to risk factors.

# Risk Factors

## Cervical cancer

### 1. Human Papilloma Virus (Hpv) Infection:

Human Papilloma virus is an established risk factor and etiology of developing invasive cervical cancer. A high prevalence of human papillomavirus (HPV) 16 and 18 in cervical cancer specimens have been shown in India.(13) In respect to HPV type, the association of cervical carcinoma with HPV 18 seemed to be somewhat stronger than the one with HPV 16. Compared to other high-risk types, HPV 18 has been associated with increased oncogenic potential in cell culture, faster transition to invasive cancer and poorer prognosis.(14,15)

**2. Poor Socio-Economic Status And Poor Hygeine:**

Cervical cancer is more prevalent in less developed nations and has significant correlation with poor socio-economic status and poor genital hygiene. A direct role of poor hygienic conditions on risk of HPV infection and cervical cancer has been reported.(16)

**3. Early Age At First Sexual Intercourse:**

Early age at first sexual intercourse has been associated with an increased risk of high-risk human papillomavirus (HPV) infection, a sexually transmitted infection, that in susceptible women is responsible for virtually all cases of invasive cervical cancer. Age at first marriage is often used as a proxy measure for age at first sexual intercourse.(17)

**4. Cigarette Smoking:**

Tobacco smoke is a well-established human papillomavirus (HPV) cofactor for the development of cervical precancer and cancer. (18) Acquisition of high-risk HPV infection seems to be a smoking independent event; however, progression of the acquired infection is negatively affected by current smoking. Association of developing cervical cancer in former smokers is not well established. The mechanisms of smoking on HPV driven cervical carcinogenesis seem to be complex and multifactorial.(19)

**5. Sexually Transmitted Disease and HIV Infection:**

Serologic evidence of previous sexually transmitted disease like syphilis, herpes simplex type 2 infection and chlamydial infection were predictors of developing invasive cervical carcinoma.(20) Most important risk factor for cervical cancer development is chronic persistent HPV infection. Women with HIV are more likely to have persistent HPV infection leading to cervical abnormalities and cancer.(21) In 1993, cervical cancer became an AIDS defining illness among women with HIV.(22)

## Endometrial Cancer

**1. Age :**

Endometrial cancer risk is found to be positively correlated with increasing age. As endometrial cancer is more common in post-menopausal women than in premenopausal women, over 90% of the cases are diagnosed after the age of 50 years. Advanced age is also considered as a predictor of poor outcome in patients with endometrial cancer. (23–25)

2. **Race:**

Data from USA showed differences in the incidence of endometrial cancer and mortality rate among races. White women have a higher risk of developing endometrial cancer than women belonging to other ethnic groups.(8) Endometrial cancer has a higher incidence in White Americans when compared to African Americans, Native Hawaiians, Japanese Americans, and Latinas. However, in comparison with other races the mortality rate in white women is the lowest. Different incidence rates of endometrial cancer among races could be due to differences in life-style, socioeconomic status, and genetic predisposition to developing cancers.(25)

3. **Early Menarche & Late Menopause:**

Early age at menarche and late age at menopause are positively associated with some female cancers. Breast, endometrial and ovarian cancer were all found to be affected by degree of exposure to oestrogen.(26) Earlier menarche increases the risk of developing endometrial cancer up to 9 fold compared with woman whose menarche occurred at or above the age of fifteen year.(27)

4. **Family History :**

About 5% of endometrial cancer cases have a family history of the disease among first degree relatives**.** (28) Family history of endometrial cancer is associated with increased disease risk from two to three fold among

premenopausal women. (29) In women less than 50 years old, about 9% of endometrial cancer is due to mutations in mismatch repair genes (MSH1, MSH2, MSH6), which result in Hereditary Non-Polyposis Colorectal Cancer (HNPCC) also known as Lynch II syndrome. Endometrial cancer is considered to be the second most common cancer in HNPCC and the average age of diagnosis of endometrial cancer has been reported to be between 46 and 62 years old (30). These mutations raise the lifetime risk of endometrial cancer risk up to 60% by the age of 70 years. (31)

5. **History of other Female Cancers:**

A woman who has a history of other cancers has a three fold increase in the risk of developing endometrial cancer, compared with woman with no history of cancer. Women who had breast or ovarian cancer are at increased risk of developing endometrial cancer (32,33). Uterine cancer risk increases 2.7 fold among BRCA1 carriers, which is less than the effect on the risk of breast cancer (33), while no increase in risk is found in BRCA2 mutation carriers.(34)

6. **Nulliparity And Infertility:**

Lower parity and/or nulliparity were found to increase the risk of developing endometrial cancer up to four fold, while multiparity decreases the risk of endometrial cancer up to 70% (35). Elevated serum

oestrogen levels is one of the main feature associated with chronic anovulation, and this creates enough reason to increase the risk of developing endometrial cancer . Thus, women with Polycystic Ovary Syndrome (PCOS) and women with oestrogen-secreting ovarian tumours are more prone to have endometrial cancer especially in their reproductive life. (36)The effect of infertility on endometrial cancer is well documented, as it puts the patients at risk of developing endometrial cancer at a younger age(37)

**7. Postmenopausal Hormone Therapy:**

Oestrogen Therapy (ET) is the use of oestrogen alone to offset the symptoms of menopause. In the past oestrogen was used alone to treat symptoms of menopause such as hot flushes. Endometrial cancer is associated with a high level of exposure to oestrogen, and the use of oestrogen alone increases the risk of endometrial cancer fivefold as it delays the age of menopause. (38–40)

**8. Obesity:**

Obesity is a well identified risk factor for endometrial cancer, both in pre-menopausal and post-menopausal women . The risk of endometrial cancer becomes higher when obesity is associated with infertility or amenorrhea (41). Endometrial cancer risk increases by 1.2-fold for each 5 kilograms

weight gain . Obese premenopausal women have a more than 7-fold increased risk of developing endometrial cancer compared to obese postmenopausal women(42).

**9. Tamoxifen :**

Tamoxifen is a selective oestrogen receptor modulator often used to treat women with an oestrogen receptor positive breast cancer (43). Tamoxifen stimulates endometrial proliferation and as the duration of treatment increases the thickness of the endometrium increases (44). Endometrial cancer risk increases with the duration of tamoxifen use with a relative risk of 2.0 for 2–5 years and 6.9 for at least 5 years when compared to non-users (44).

10. **Diabetes:**

Recent studies (41,45,46) have shown a positive relationship between endometrial cancer risk and diabetes. In comparison with non-diabetic woman, a diabetic woman has a 2 to 3-fold increased risk of developing endometrial cancer. Obesity can exaggerate the effect of diabetes, as most patients with Type II diabetes are obese. Friberg and colleagues found a more than 6-fold increase in the risk of endometrial cancer when diabetes is associated with obesity.(45)

# RISK FACTORS OF ENDOMETRIAL CARCINOMA

| Risk factor | Relative risk |
|---|---|
| Increasing age | NA |
| Unopposed estrogen therapy | 2 to 10 |
| Late menopause (after age 55) | 2 |
| Nulliparity | 2 |
| Polycystic ovary syndrome (Chronic anovulation) | 3 |
| Obesity | 2 to 4 |
| Diabetes Mellitus | 2 |
| Hereditary non polyposis colorectal cancer | 22 to 50 percent lifetime risk |
| Tamoxifen | 2/1000 |

NA = Relative risk not reported

Table 1: Risk factors of endometrial carcinoma. Adapted from Smith, R. A et al (2001), American Cancer Society Guidelines for the Early Detection of Cancer: Update of Early Detection Guidelines(47)

# Clinical Anatomy

## Uterine Cervix

### Primary site

The cervix is the lower aspect of the uterus. It is roughly cylindrical in shape, projects through the superior-anterior vaginal wall, and communicates with the vagina through the endocervical canal, which terminates in the external os located at the top of the vagina. Cancer of the cervix may originate from the mucosa of the surface of the cervix or from within the canal. Carcinoma of the uterine cervix grows locally and may extend in continuity to the uterus and paracervical tissues, and pelvic organs.

### Nodal spread

Cervical cancer may spread to regional lymph nodes, and only later metastasize hematogenously to distant structures. Studies on sentinel lymph nodes show that the cervix is drained into the following first echelon nodal stations most commonly: external iliac (43%), obturator (26%) and parametrial (21%), from where they drain to the common iliac nodes. From the common iliac nodes, lymph drainage goes to the para-aortic nodes.

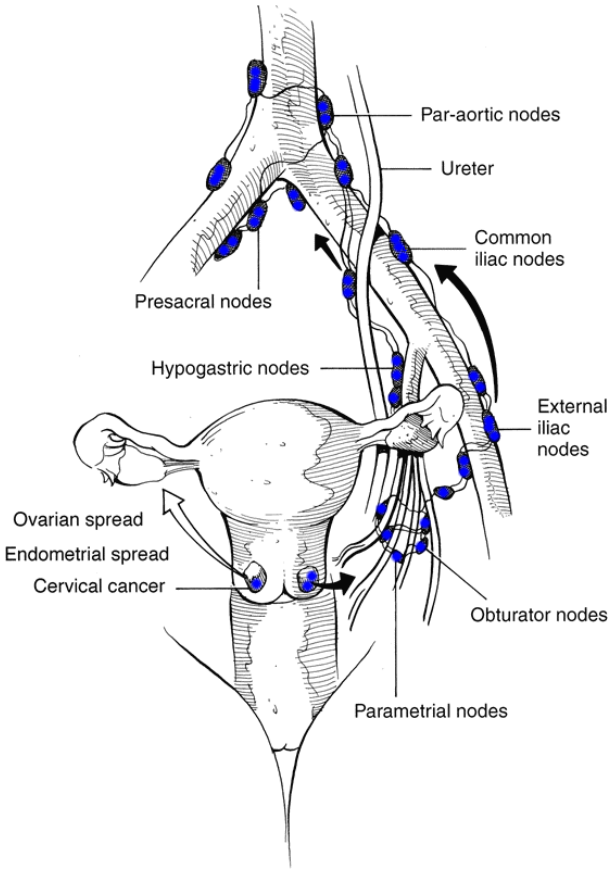



Fig 4: Patterns of nodal spread in cervical cancer. (48)

**Metastatic sites**

The most common sites of distant spread include the mediastinal and supraclavicular nodes, the lungs, liver, and skeleton.

## Uterine Corpus

**Primary site**

The upper two-thirds of the uterus above the level of the internal cervical os is called the corpus. The fallopian tubes enter at the upper lateral corners of a pear-shaped body. The portion of the muscular organ that is

above a line joining the tubo-uterine orifices is often referred to as the fundus.

**Nodal stations**

The major lymphatic trunks are the utero-ovarian (infundibulopelvic), parametrial, and presacral, which drain into the hypogastric, external iliac, common iliac, presacral, and para-aortic nodes. Although a direct route of lymphatic spread from the corpus uteri to the paraaortic nodes through the infundibulopelvic ligament has been suggested from anatomical and sentinel lymph node studies, direct metastases to the para-aortic lymph nodes are uncommon.

**Metastatic sites**

The peritoneum and lungs are the common metastatic sites.

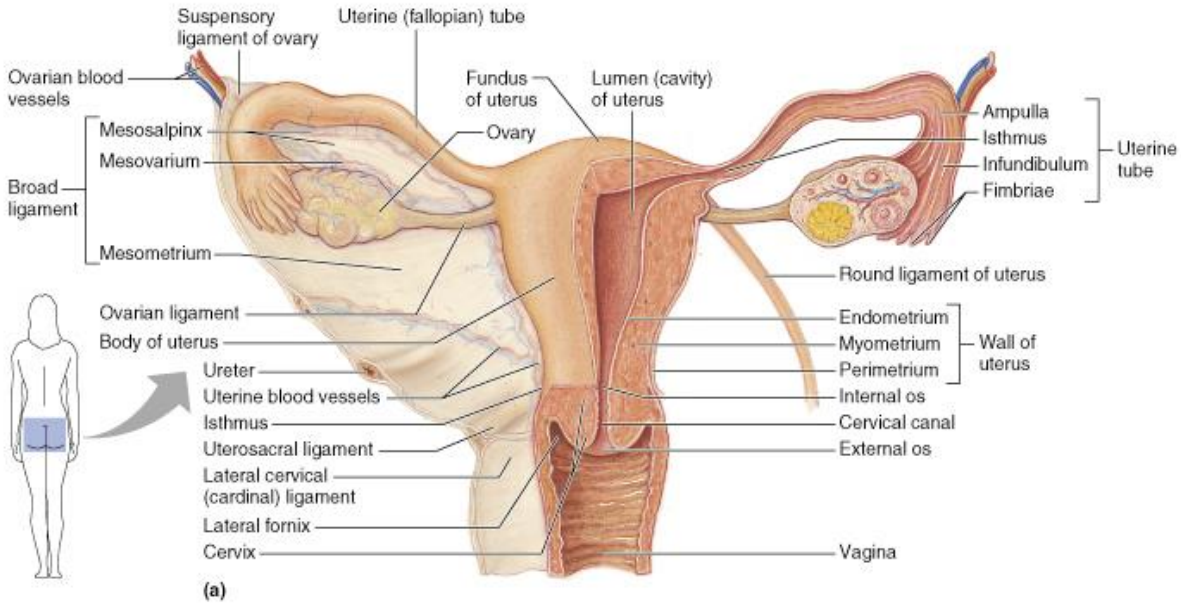



Fig 5: Anatomy of female reproductive organ

## Figo Staging of Cervical Cancer (2018 update)

| Stage | | Clinical Finding |
|---|---|---|
| I | | The carcinoma is strictly confined to the cervix (extension to the uterine corpus should be disregarded). |
| IA | | Invasive cancer identified only microscopically. (All gross lesions even with superficial invasion are Stage IB cancers.) Invasion is limited to measured stromal invasion with a maximum depth of 5 mm and no wider than 7 mm. |
| | IA1 | Measured invasion of stroma ≤ 3 mm in depth and ≤ 7 mm width. |
| | IA2 | Measured invasion of stroma > 3 mm and ≤ 5 mm in depth and ≤ 7 mm width. |
| IB | | Clinical lesions confined to the cervix, or preclinical lesions greater than stage IA. |
| | IB1 | Clinical lesions no greater than 4 cm in size. |
| | IB2 | Clinical lesions ≥ 4 cm in size. |
| II | | The carcinoma extends beyond the uterus, but has not extended onto the pelvic wall or to the lower third of vagina. |
| IIA | | Involvement of up to the upper 2/3 of the vagina. No obvious parametrial involvement |
| | IIA1 | Clinically visible lesion ≤ 4 cm |
| | IIA2 | Clinically visible lesion > 4 cm |
| IIB | | Obvious parametrial involvement but not onto the pelvic sidewall. |
| III | | The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney and/or involves pelvic and/or para-aortc lymph nodes |
| IIIA | | Involvement of the lower vagina but no extension onto pelvic sidewall. |
| IIIB | | Extension onto the pelvic sidewall, or hydronephrosis/non-functioning kidney. |

| | | |
|---|---|---|
| IIIC | IIIC1 | Pelvic lymph node metastasis only |
| | IIIC2 | Para-aortic lymphnode metastases |
| IV | | The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. |
| IVA | | Spread to adjacent pelvic organs. |
| IVB | | Spread to distant organs |

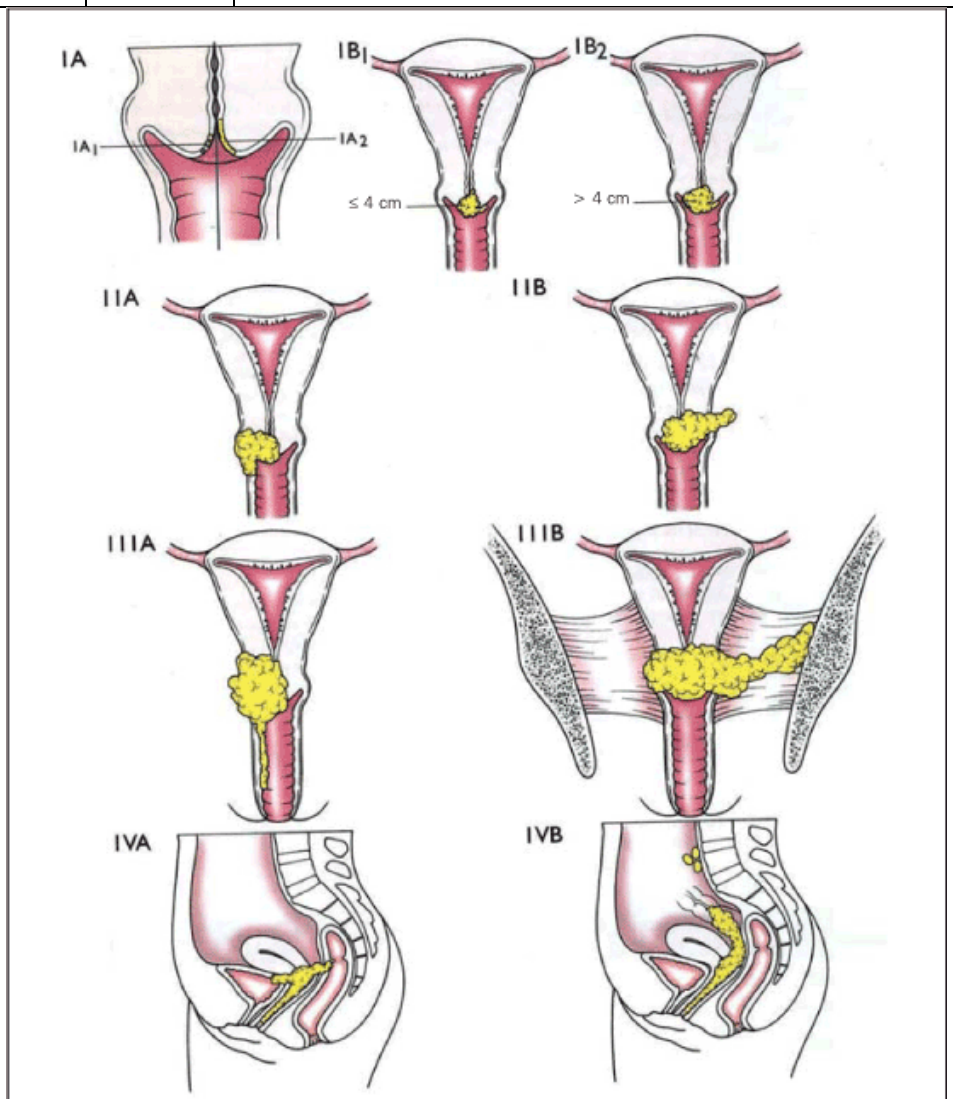



Fig 6 : FIGO staging of cervical cancer.
Ref: Internet - https://myradnotes.wordpress.com/cervical-cancer-staging/

## Histological Subtypes

*Squamous cell carcinoma* comprises of more than 90% of cervical cancers. Squamous cell carcinoma is composed of cores and nests of epithelial cells arranged randomly and cells show central keratinization with pearls. Squamous cell carcinomas are divided into three types: large-cell keratinizing, nonkeratinizing, and small-cell carcinomas.(48)

*Verrucous carcinoma* is a variant of a very well differentiated squamous cell carcinoma that characteristically has a tendency to recur locally but not to metastasize.

*Adenocarcinoma* arises from the cylindrical mucosa of the endocervix or the mucus-secreting endocervical glands. Mucinous is the most common subtype of adenocarcinoma. Sometimes it is difficult to differentiate a primary endocervical adenocarcinoma from an endometrial tumour. Drescher et al. described a higher incidence of involvement of the uterine corpus and the regional lymph nodes in 21 patients with adenocarcinoma compared with a similar number of patients with squamous cell carcinoma.(49)

*Adenoma malignum* is a rare form of cervical cancer that is difficult to diagnose, and often highly malignant and refractory to treatment. Adenoma malignum is associated with Peutz-Jeghers syndrome and has an ominous natural history, with few reported cures.

*Adenoid cystic carcinoma* is a rare variant of adenocarcinoma of the cervix (<1%), with an appearance similar to its counterparts in the salivary gland or the bronchial tree. The tumour is composed of nests and nodules of small carcinoma cells with a few characteristic cribriform patterns. They are locally aggressive and prone to metastasize.(50,51)

## Screening for Cervical Cancer

Screening is effective method to prevent and reduce in incidence of cervical cancer but most women in poor countries do not have access to effective screening programmes. Up to 50 percent of sexually active young women will have positive HPV tests within 36 months of first sexual activity, and up to 57 percent of sexually active female adolescents are infected with HPV at any one point in time.

Most women will clear the HPV infection within 8 to 24 months; particularly in adolescents and young women, HPV infections and dysplasia are likely to resolve spontaneously. In a cost-effectiveness, study of different cervical screening approaches in India and other developing countries, screening women once a lifetime, at the age of 35 years, with a one- or two-visit screening strategy involving VIA or HPV testing reduced the lifetime risk of cancer by approximately 25–36% and cost less than 500 US dollars per year of life saved. The relative cancer

risk declined by an additional 40% with two screenings (at 35 and 40 years of age) (Goldie et al., 2005). Of all the screening tests available, the three main cervical cancer screening procedures commonly employed in India are Papanicolaou smears (Pap smears)/ liquid base cytology, visual inspection with acetic acid (VIA) and HPV DNA testing.

Pap smear is conventional cytology methods to identify abnormal cells sampled from the transformation zone, the junction of the ecto- and endocervix, where cervical dysplasia and cancers arise. Liquid based cytology can be done with a specially designed brush which used to sample cells from ectocervix and endocervix and it is transported in a liquid medium.

VIA involves naked eye inspection of the uterine cervix after application of dilute acetic acid to visualize definite, opaque acetowhite lesions close to the squamocolumnar junction. VIA can be provided by a variety of personnel such as trained nurses, midwives and health workers. Recent studies indicate that it has a sensitivity ranging from 70 to 85% in detecting high-grade cervical intraepithelial neoplasia (CIN 2–3) and invasive cancer.

HPV nucleic acid PCR method has become a standard, non-invasive method for screening cancer screening. HPV molecular tests increase the sensitivity of cervical cancer screening programs by detecting high-risk lesions earlier in women 30 years and older with normal cytology. HPV DNA, HPV mRNA and HPV E6 protein are molecular tests used to detect high risk HPV. HPV DNA PCR testing is commonly used and is highly sensitive compared to Pap smear and VIA.

## Figo Staging of Endometrial Cancer (2015)

| **Stage** | | **Clinical Finding** |
|---|---|---|
| I | | Tumour confined to the corpus uteri |
| | IA | No or less than half myometrial invasion |
| | IB | Invasion equal to or more than half of the myometrium |
| II | | Tumour invades cervical stroma, but does not extend beyond the uterus |
| III | | Local and/or regional spread of the tumour |
| | IIIA | Tumour invades the serosa of the corpus uteri and/or adnexa |
| | IIIB | Vaginal involvement and/ or parametrial involvement |
| | IIIC | Metastases to pelvic and/or para-aortic lymph nodes |
| | IIIC1 | Positive pelvic nodes |

| | | |
|---|---|---|
| | IIIC2 | Positive para-aortic nodes with or without positive pelvic lymph nodes |
| IV | | Tumour invades bladder and/or bowel mucosa, and/or distant metastases |
| | IVA | Tumour invasion of bladder and/or bowel mucosa |
| | IVB | Distant metastasis, including intra-abdominal metastases and/or inguinal nodes) |

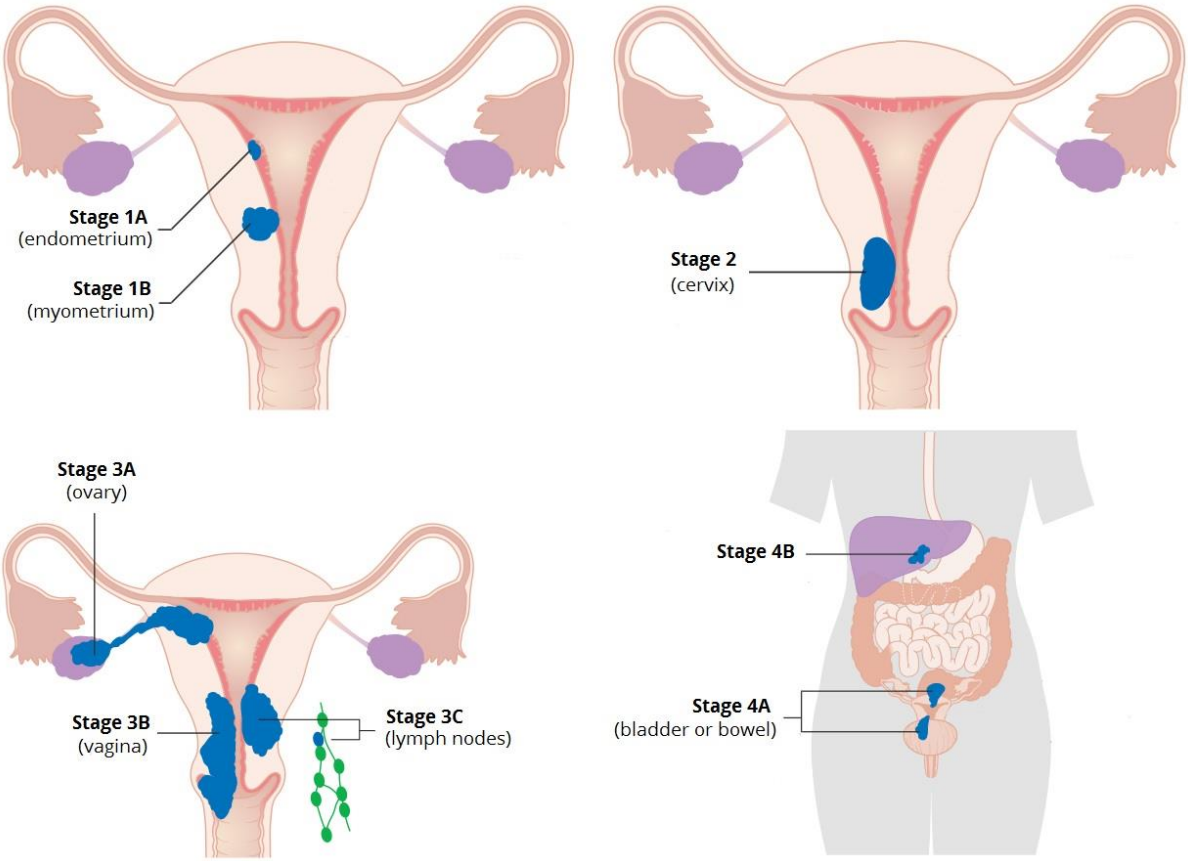



Fig 7 : FIGO staging of Endometrial cancer.

## Types of Endometrial Cancer

| Features | Type 1 | Type 2 |
|---|---|---|
| **Age** | 50 -60 years | >70 years |
| **Risk factors** | Chronic estrogen exposure, obesity, nulliparity, HNPCC | Atrophy |
| **Premalignant condition** | Atypical endometrial hyperplasia | Not well defined |
| **Histological types** | Endometroid adenocarcinoma and their variants | Clear cell and papillary serous carcinoma |
| **Genetics** | K-Ras, PTEN, MLH – 1 | P53, Erb2 |
| **Metastases** | Lymph nodal, ovarian | Peritoneal |
| **Prognosis** | Good | Poor |

Table 2 : Characteristics of types of endometrial cancers

## Histological Subtypes

**Endometrioid carcinoma** — Endometrioid histology is the most common type of endometrial cancer, accounting for 75 to 80 percent of cases. These tumours are stimulated by oestrogen, are typically are preceded by endometrial hyperplasia (also referred to as endometrial intraepithelial neoplasia [EIN]), present at an early stage, and have a good prognosis.(52)

Endometrioid carcinoma is composed of tall columnar cells lining back-to-back glands without intervening stroma. The glands have a smooth luminal contour. Cribriform (gland within a gland) patterns are also common. Occasionally, endometrioid cells have a prominent papillary or villoglandular growth pattern.(53)

Endometrioid cancers are graded using the FIGO classification system, which assesses the architectural pattern and nuclear grade:

- Grade 1 – Less than 5 percent solid growth patterns
- Grade 2 – 6 to 50 percent solid growth patterns
- Grade 3 – Greater than 50 percent solid growth

**Mucinous carcinoma** — is composed of >50 percent mucinous cells, and the remainder of the tumour shows endometrioid morphology (52).

These are type 1 tumors, which are graded using the FIGO system. These tumors are typically low grade with a good prognosis.

Biopsy results of a mucinous endometrial carcinoma may be difficult to interpret and this tumour may confused with endocervical adenocarcinoma, or a biopsy specimen may lack diagnostic features of carcinoma due to a fragmented papillary pattern of growth. There is a high prevalence of KRAS mutations in this type of tumour.

**Serous carcinoma** — Serous carcinoma is the second most common type of endometrial cancer but only accounts for about 10 percent of cases.

Most serous endometrial carcinomas have a worse prognosis, as there is frequently clinically occult extrauterine disease present at the time of diagnosis. Serous carcinomas often diffusely infiltrate the myometrium and may have extensive lympho-vascular space invasion and peritoneal spread, similar to ovarian carcinoma.

**Clear cell carcinoma** — Clear cell EC is an uncommon histologic type (<5 percent) of endometrial cancer. Like serous carcinoma, this tumour is typically high grade and often presents at an advanced stage.

**Carcinosarcoma (malignant mixed mullerian tumour)** — Carcinosarcomas are rare endometrial carcinomas (<5 percent) that

contain both a malignant epithelial component (carcinoma) and a malignant stromal component (sarcoma). They often form a large polyp, completely filling the endometrial cavity. The sarcoma component may be composed of cell types usually seen in the uterus, such as smooth muscle and endometrial stroma (homologous tumors), or unusual tissue such as cartilage, bone, and skeletal muscle (heterologous tumors).

| Histology | Proportion of endometrial carcinoma (%) |
|---|---|
| Endometrioid | 77 |
| Mucinous | 1 |
| Serous | 7 |
| Clear cell | 2 |
| Mixed cell type | 8 |
| Carcinosarcoma | 4 |

Table 3 – Steinhoff M, Brown University, 2016. Data from 1300 cases from Women and Infants Hospital Cancer Registry 2010-2014, Providence, Rhode Island

## Screening for Endometrial Cancer

According to American Cancer Society guidelines for detection of early cancer, no routine screening strategies were recommended. Women at average risk should be informed about risks and symptoms of endometrial cancer, and strongly encouraged to report any symptom. American

Cancer Society recommends that annual screening for endometrial cancer with endometrial biopsy should be offered by age 35 for women with or at risk for hereditary nonpolyposis colorectal cancer (HNPCC). (47)

## Surgical Management of Cervical Cancers

*Stage1A1* - In an extensive review of the literature, Ostor et al reported that of 2,274 squamous lesions with invasion of less than 3 mm, only eight cases had lymph node metastases (0.5%). A cone biopsy with clear surgical margins should be considered adequate treatment for a patient with stage IA1 squamous carcinoma of the cervix. Many patients with early cervical cancer are young, and preservation of fertility is a major concern. Consequently, surgical approaches that remove the primary lesion and regional lymph nodes, while conserving the corpus for future childbearing, have been explored. If future childbearing is not required, then extrafascial hysterectomy may be considered. This should be the treatment of choice in postmenopausal women because stenosis of the endocervical canal is common after conization, which limits the ability to obtain endocervical cytology.

*Stage 1B2* - In patients who prefer to preserve fertility, radical trachelectomy +/- laparoscopic pelvic lymphadenectomy is recommended and has been found to have the least complication rates. If the patient does

not require fertility preservation, the recommended treatment for stage IA2 squamous carcinoma of the cervix is modified radical hysterectomy and pelvic lymph node dissection.

*Stage 1B1 and early IIA* - Patients with stage IB1 are universally regarded as being ideal candidates for radical hysterectomy and pelvic lymphadenectomy, although equal cure rates may be obtained with primary radiation therapy.(54) Primary surgery has the advantage of removing the primary disease and allowing accurate surgical staging, thereby allowing any adjuvant therapy to be more accurately targeted. As toxicity increases with multimodality treatment, patient selection is vital before offering primary surgery in high risk cases.

## Surgical Management of Endometrial Cancers

The cornerstone of treatment for endometrial cancer is total hysterectomy and bilateral salpingo-oophorectomy +/- Pelvis lymphadenectomy + Omentectomy. Surgical staging (Pelvic lymphadenectomy + Omentectomy) is recommended for all stages of endometrial cancers but often decision is made intra-operatively based on findings of frozen section. (55) Preoperative scans cannot detect micrometastases in lymphnodes, hence complete lymphadenectomy is recommended. Sampling is not encouraged as it may lead to inaccurate information. In a

large SEER data analysis published by Chan et al., it was reported that the removal of more than 20 lymph nodes significantly increased the probability of detecting at least one positive lymph node in endometrioid uterine cancer and significantly improved 5-year disease specific survival in high risk groups. Lutman et al., reported that the pelvic lymph node count was an important prognostic variable for patients with FIGO stages I and II endometrial carcinoma and high-risk histology.(56,57) However, no significant benefit of lymph node resection in low-risk patients could be demonstrated. (58) Performing lymphadenectomy in this low-risk cohort dramatically increases morbidity and cost of care without any discernible benefit. An extensive para-aortic lymphadenectomy significantly increases operating time, blood loss, and postoperative morbidity, particularly lower limb lymphedema and hence it is not routinely practiced. Para-aortic nodal sampling is usually done in patients with enlarged or suspicious para-aortic nodes. Sentinel node mapping can be a reasonable alternative to strike a balance between systematic lymphadenectomy and no dissection at all in low and intermediate risk endometrial cancer.(59)

## Prognostic Factors and Adjuvant Therapy

Although surgery is the mainstay of treatment for early cervical and endometrial cancers, significant local recurrences were noted in certain subgroup of patients.

### Cervix

In 1981, Rotman et al published an editorial review based on retrospective data which suggested that certain histo-morphologic characteristics such as depth of tumor, presence of vascular invasion, endocervical growth, tumor extending into the lower uterine segment, or barrel-shaped tumors seem to worsen prognosis in patients with early cervical carcinoma. He also suggested that these factors may be related to increased incidence and early lymphatic spread and ultimately, locoregional failure(60). This paved way for multiple prospective trials evaluating the patterns of local and locoregional recurrences and multimodality management of the same.

Sufficient data had been reported in the literature to categorize tumour size, deep stromal invasion, and lymphovascular invasion as independent risk factors contributing to local recurrence and mortality(61–64). Gynecologic Oncology Group (GOG) in 1999 published a landmark randomized control trial which evaluated the role of adjuvant radiation therapy in carcinoma cervix stage I B after radical hysterectomy and

pelvic lymphadenectomy(1). According to Sedlis et al, any two of three risk factors are indication of adjuvant radiation therapy or any non-squamous histology.

A. Sedlis criteria (any 2 out of 3)

   i. Lymphovascular invasion

   ii. Deep stromal invasion (>1/3 stromal invasion)

   iii. Tumour size > 4cms

B. Non-squamous histology

A long-term follow-up results of GOG 99 study published by Martin & Sedlis et al suggested the role of adjuvant radiation therapy in improving progression free survival and local control in early stage cervical cancer after radical hysterectomy. Adjuvant radiation therapy was proven to be beneficial in patients with high risk factors and adenocarcinoma/adenosquamous histology with acceptable grade 3/4 toxicities(2). But overall survival benefit with radiation therapy failed to have statistical significance. Cochrane Meta-analysis published in 2009 and 2014 established the role of adjuvant radiation therapy in decreasing the risk of disease progression compared with no further treatment, but little evidence that it might improve overall survival, in stage IB cervical cancer. (65,66)

## Endometrium

In 1980, Aalders et al published prospective trial which was one of the earliest trial that evaluated the role of radiation therapy in stage 1 endometrial cancer.(67) Three significant phase III randomized controlled trials including the Post-Operative Radiation Therapy in Endometrial Cancer (PORTEC) -1,2 and Gynaecologic Oncology Group (GOG)-99 defined high-intermediate risk group in surgically staged endometrial cancer patients and demonstrated a significant decrease recurrence rates following adjuvant radiotherapy in these population without altering overall survival.(68–71) Adjuvant radiotherapy decreased the local and locoregional rates from 25% to 5% in high intermediate risk groups. Risk factors identified from these trials are:

- Histological Grade 3
- Age 60 years or older
- Deep myometrial invasion
- Lympho-vascular invasion

ASTEC meta-analysis showed a clear local control benefit with radiation therapy in high-intermediate risk group with no significant overall survival benefit. Radiation therapy was not recommended for low to intermediate risk groups as no significant local control or survival benefit was demonstrated and higher acute and late toxicity rates.(72) Fifteen year

follow up study of PORTEC 1 showed clear benefit with radiation therapy in terms of local control and considering adjuvant radiation therapy was justified due to high local recurrence rate (>20%) in high intermediate risk groups. This study also showed a slightly higher rate of second malignancies and higher gastro-intestinal and genitourinary toxicity rates. Although current sophisticated external radiation therapy planning techniques (intensity-modulated RT) may be expected to have lower GI toxicity rates, the irradiated volume in the lower pelvis remains large, and the long-term risks of pelvic floor dysfunction, GI symptoms, and second cancers cannot be disregarded. (68)

In view of higher toxicity, PORTEC-2 trial investigated trial compared the efficacy and toxicity of external beam radiation therapy and vaginal brachytherapy for endometrial cancer of high-intermediate risk. At a median follow up of 45 months, similar local control rates and very few vaginal recurrences were seen in both arms. Hence, established the fact that vaginal brachytherapy was equally effective in achieving local control. Lower gastro-intestinal and genitourinary toxicity rates was noted in vaginal brachytherapy as compared to external radiation therapy. Vaginal toxicity (stenosis, atrophy) was higher in brachytherapy in view of high dose to vaginal surface. (70)

In a recent health related quality of life and survivorship evaluation of PORTEC 2 trial patients, patients who received external beam radiation therapy had more bowel symptoms with impact on daily activities. A trend for more urinary symptoms, without impact on overall quality of life or difference in cancer survivorship issues was also noted between the two arms. No difference in sexual activity was seen between treatment arms.(73)

## Vaginal Brachytherapy

After results of PORTEC 2 suggesting equivalence of vaginal brachytherapy in external beam radiation therapy in high-intermediate risk group of endometrial cancers, the practice of vaginal brachytherapy increased (74). Vaginal brachytherapy is also used in cervical cancers but often as a boost to external beam radiation therapy. Vaginal cuff boost should be considered in patients with a less than radical hysterectomy, close or positive margins, large or deeply invasive tumours, parametrial or vaginal involvement, or extensive lympho-vascular invasion. American Brachytherapy Society published guidelines in 2012 for vaginal cuff brachytherapy based on existing data and evidence.

*Pretherapy evaluation:* A complete pelvic examination should be performed, and it must be determined that the vaginal cuff has healed

before the therapy and that small bowel has not herniated through the vaginal apex. Adjuvant brachytherapy is usually not performed until at least 4 weeks have elapsed since surgery. The increasing use of robotic or laparoscopically assisted vaginal hysterectomies may decrease the amount of time necessary for adequate healing of the vaginal cuff.

*Applicators:* A vaginal cylinder or ovoids are commonly used for post-hysterectomy adjuvant brachytherapy of the vaginal cuff. Ovoids treat only the upper part of the vaginal (vaginal cuff), whereas vaginal cylinder allows treatment of the entire length of the vagina. Single channel cylinders have been shown to deliver a higher dose to the bladder and rectum for a given vaginal dose compared with ovoids, but this problem may be ameliorated by the use of a multichannel cylinder. Vaginal ovoids can lead to underdosage at the central apex of the vagina if there is significant separation and a heterogeneous dose may occur depending on the specific packing used. Also, ovoids do not adequately treat the lower vaginal area. Thus, there are advantages and limitations to each type of applicator system.

*Cylinders:* The ABS recommend that institutions should have available vaginal cylinders in various lengths and diameters (ranging from 2.0 to 4 cm). Individual cylinders of predetermined lengths, or segmented cylinders that can be assembled to the required length, are available. Most

vaginal cylinders have a single, central channel. The multichannel vaginal applicator contains a central channel and six peripheral channels along the surface of the cylinder.

*Dose & fractionation:* According to vaginal brachytherapy survey (2014), 7 Gy x 3 fractions prescribed to 0.5 cm is a common fractionation scheme.(75) Lower LDR equivalent doses namely 6 Gy x 5 (MD Anderson regimen) or 4 Gy x 6 (Dana-Farber/Brigham and Women's regimen) to the surface have shown good results. The most common fractionation for VBT as a boost after EBRT is 5 Gy for three fractions to 0.5-cm depth. More than 50% of the practitioners in US treat twice a week.

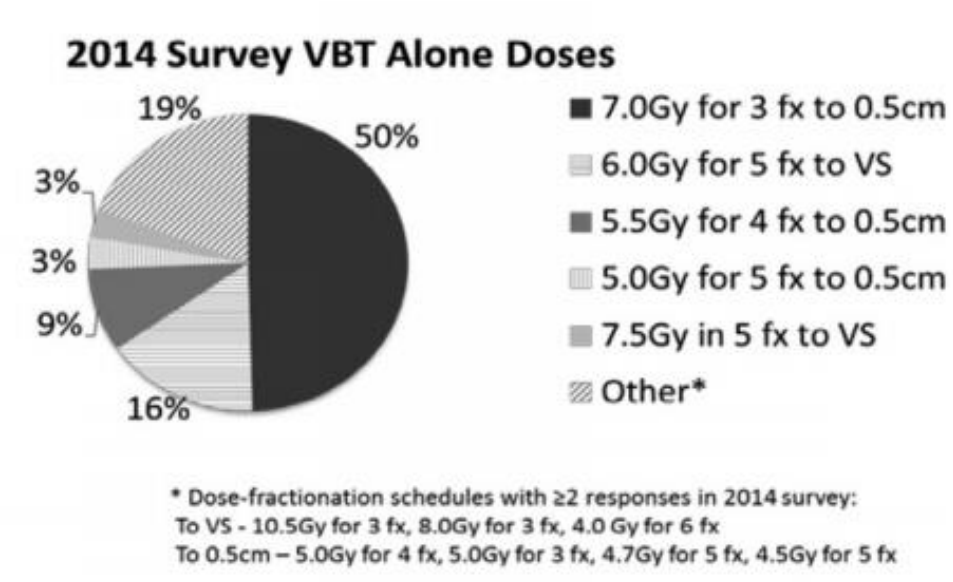



Fig 8: VBT alone doses in clinical practice based on ABD 2014 survey

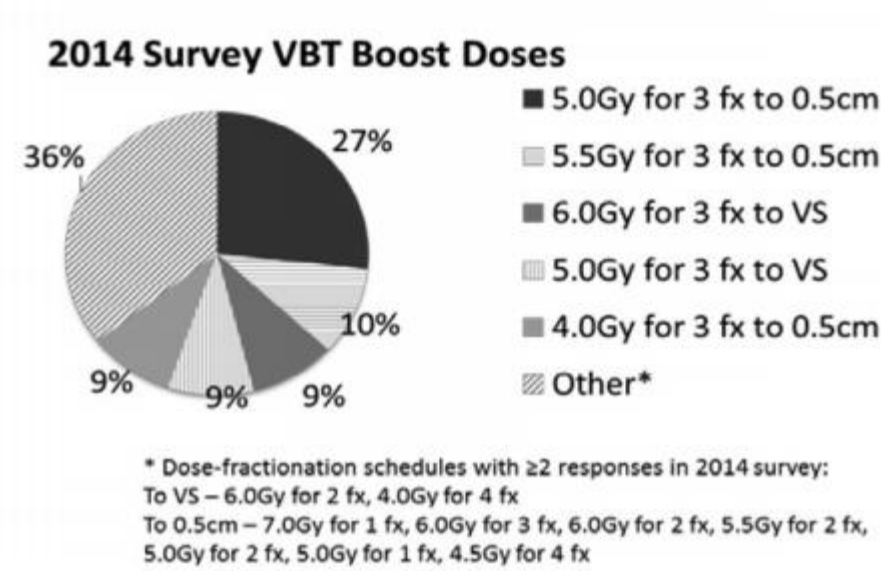



Fig 9: VBT boost doses in clinical practice based on ABD 2014 survey

## CT based 3 D planning in Vaginal brachytherapy

Most of the published data for vaginal brachytherapy using single channel cylinder applicators have been based on plain-film radiograph derived plans or library plans (76). Standard loading radiograph-based dosimetry is widely practiced in various centers around the world. In this era of image-based brachytherapy, the primary goal is to achieve the optimum dose to target while keeping the OAR doses as low as possible. Especially following conformal radiation therapy or intensity modulated radiation therapy (IMRT), image based vaginal cuff brachytherapy boost is warranted to compute normal tissue doses and target volume coverage. Image-based 3D treatment planning for brachytherapy aid in visualizing

the precise placement of cylinder in relation to vaginal surface and plan personal treatment with the knowledge of doses to the normal tissues.

In post-operative radiation therapy, sigmoid and small bowel predominantly lie in the pelvis due to lack of uterus. Hence, bladder, sigmoid and bowel are vulnerable to radiation effects in view of their close proximity to the applicator. The distance of bowel and sigmoid from the applicator in full bladder and empty bladder state is shown in Figure 10 and Figure 11.

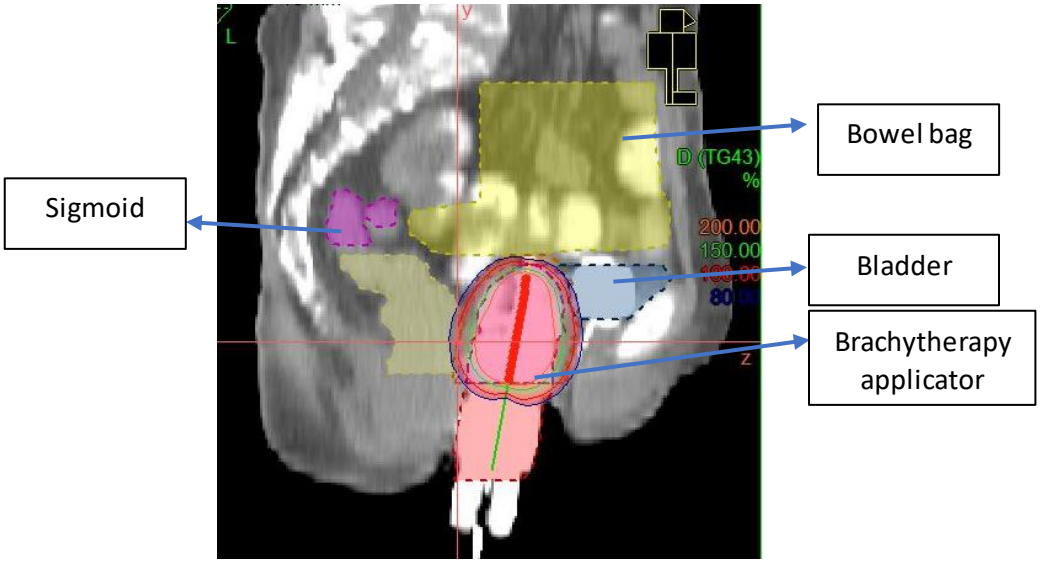



Fig10: Vaginal brachytherapy planned in empty bladder - Sagittal image

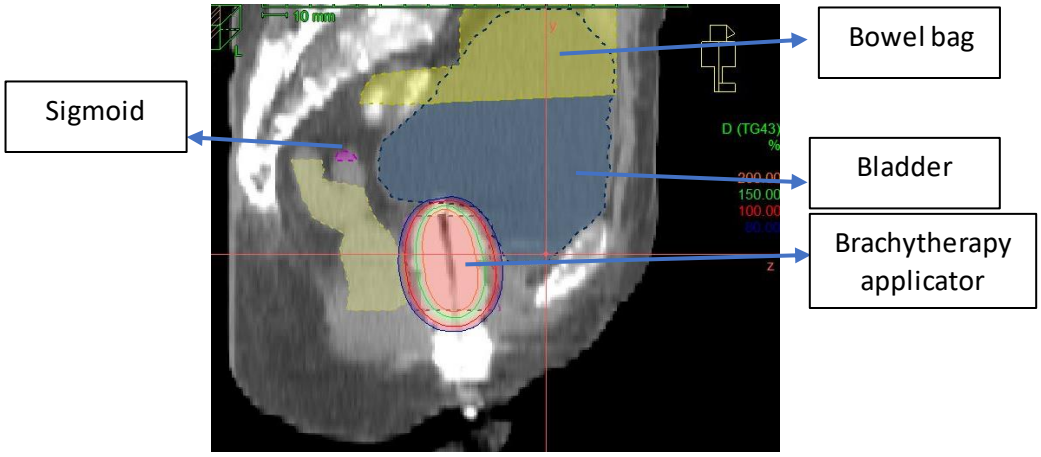



Fig11: Vaginal brachytherapy planned in full bladder - Sagittal image

Theoretically, multichannel cylinders may provide more conformal dosimetry and better compensate for single line source anisotropy at the vaginal apex. Differential loading of the channels can also potentially reduce the dose to the normal tissues compared with the single channel cylinder.

Hence, this study was taken upon to assess and compare an optimised volumetric plan to a conventional standard loading plan and evaluate if there is any advantage of a CT-based plan over the conventional library-based plan. In view of paucity of data, effect of bladder distension on critical organs like sigmoid colon and small bowel were also assessed in this study.

# MATERIALS & METHODS

## Patients

Between April 2017 to February 2018, 43 patients who were planned for post-operative vaginal mould brachytherapy were recruited in this prospective study after approval from institutional review board. All patients enrolled in this study had undergone modified radical hysterectomy +/- pelvic & para-aortic nodal dissection and had histopathological diagnosis of cervical or endometrial malignancy requiring adjuvant radiation therapy in view of high-risk factors. All patients underwent gynaecological examination to assess the vaginal vault, vaginal length and to determine the applicator diameter prior to radiation therapy planning. Written informed consent was obtained from each patient prior to participation in the study.

### Inclusion criteria

Patients with indications for adjuvant RT with the following condition:

1. Post hysterectomy status – Carcinoma Cervix

i. Sedlis criteria (any 2 out of 3)

a) Lymphovascular invasion

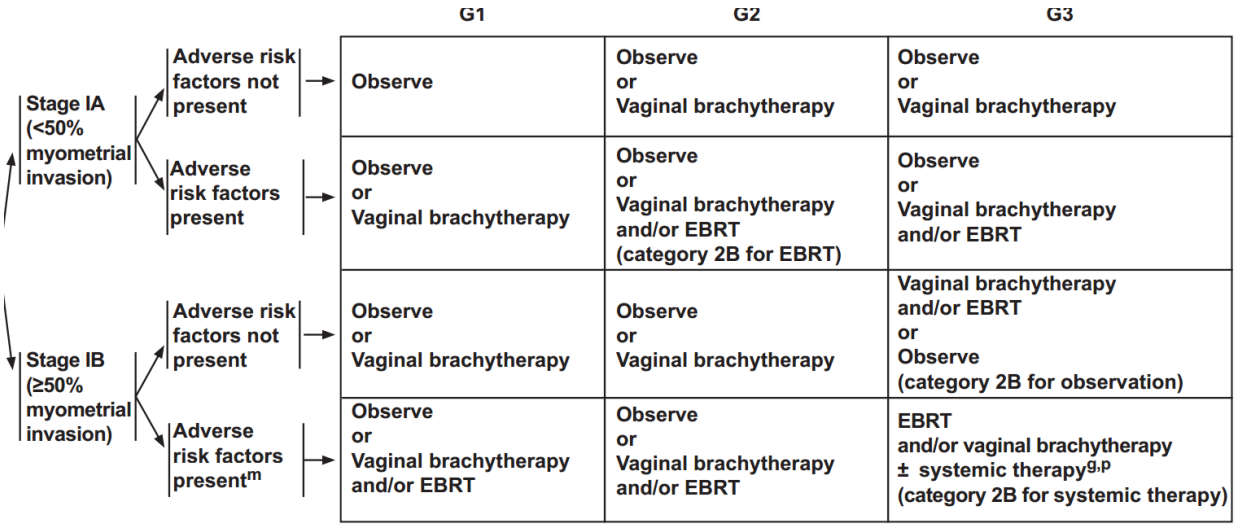
b) Deep stromal invasion (>1/3 stromal invasion)

c) Size > 4cms

ii. Sub-optimal surgery

2. Post hysterectomy status - Endometrial carcinoma (high intermediate risk)

Based on NCCN guidelines 2016



| | | G1 | G2 | G3 |
|---|---|---|---|---|
| Stage IA (<50% myometrial invasion) | Adverse risk factors not present | Observe | Observe or Vaginal brachytherapy | Observe or Vaginal brachytherapy |
| | Adverse risk factors present | Observe or Vaginal brachytherapy | Observe or Vaginal brachytherapy and/or EBRT (category 2B for EBRT) | Observe or Vaginal brachytherapy and/or EBRT |
| Stage IB (≥50% myometrial invasion) | Adverse risk factors not present | Observe or Vaginal brachytherapy | Observe or Vaginal brachytherapy | Vaginal brachytherapy and/or EBRT or Observe (category 2B for observation) |
| | Adverse risk factors present[m] | Observe or Vaginal brachytherapy and/or EBRT | Observe or Vaginal brachytherapy and/or EBRT | EBRT and/or vaginal brachytherapy ± systemic therapy[g,p] (category 2B for systemic therapy) |

3. Post hysterectomy status (for non-malignant indications) – Vaginal stump carcinoma

**Exclusion criteria**

i) Vaginal recurrences

ii) Interstitial brachytherapy planned

iii) Metastatic disease

iv) Pregnant women

## Planning CT protocol

All patients underwent a planning CT with vaginal mould applicator in treatment position. A single line source vaginal cylinder applicator with

stackable cylinders was used for all patients. Each cylinder was 2.5cms in length and a maximum for 4 cylinders could be used. Cylinder diameters from ranging from 2cm to 3.5 cm were used and widest cylinder that the patient could comfortably accommodate was inserted to obtain optimal coverage. A bladder protocol was followed for each CT. For the first CT, distended bladder protocol was followed where 1 hour prior to CT, the patient was asked to drink 1 litre of water and asked not to void until planning CT is completed. For the second CT, empty bladder protocol was followed where, under aseptic precautions, a Foley's catheter was inserted with 7cc of contrast material filled in the balloon and urine was drained completely or the patient was asked to void completely before the planning CT. Catheterisation with Foley's was discontinued to decrease discomfort and the morbidity of catheter placement because most patients were able to complete the entire procedure without the need for catheterization. Planning CT was taken from lumbosacral junction or from the iliac crest to below the ischial tuberosities at slice thickness of 3mm with extended FOV of 500cms.

## Contouring of target and organs at risk

CT images were transferred to Eclipse® contouring system (Version 13.6) and bladder, rectum, sigmoid colon and bowel bag are contoured

according to RTOG pelvic normal structure delineation guidelines. All CTs were contoured by one physician (primary investigator). Mould cylinder surface, treatment length and clinical target volume (CTV) were contoured. Clinical target volume to 5mm depth (CTVdepth) was defined by an isotropic 5mm margin expansion with respect to the treatment length from the applicator's surface. Clinical target volume to mould surface (CTVsurface) was defined as the volume encompassing the treatment length over the applicator's surface.

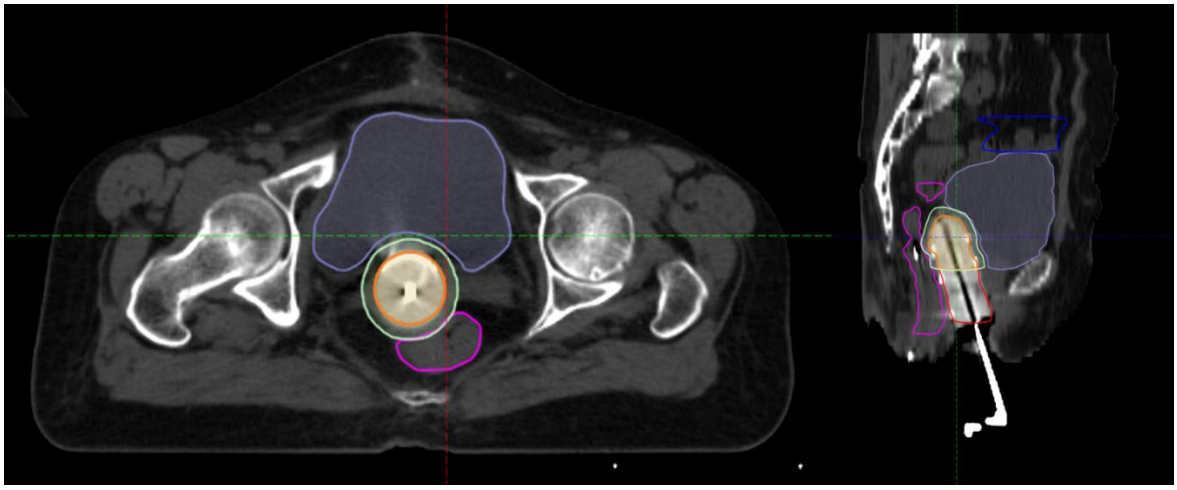


Fig12: Vaginal brachytherapy contouring – Axial and Sagittal image

## Brachytherapy planning & optimisation

CT with contoured structures were transferred to 3D treatment planning system (Oncentra® Brachy Treatment Planning Version: 4.5.3.30, Nucletron B.V., Netherlands ). Single channel of the applicator was reconstructed, and source positions were loaded to adequate length to ensure target CTV coverage.

Multiple points were generated on the CTV and dose was normalised to the same. Dose optimization were done by altering the dwell position and dwell time of the radioactive source so that minimum possible dose is delivered to the normal tissues without compromising the tumour dose.

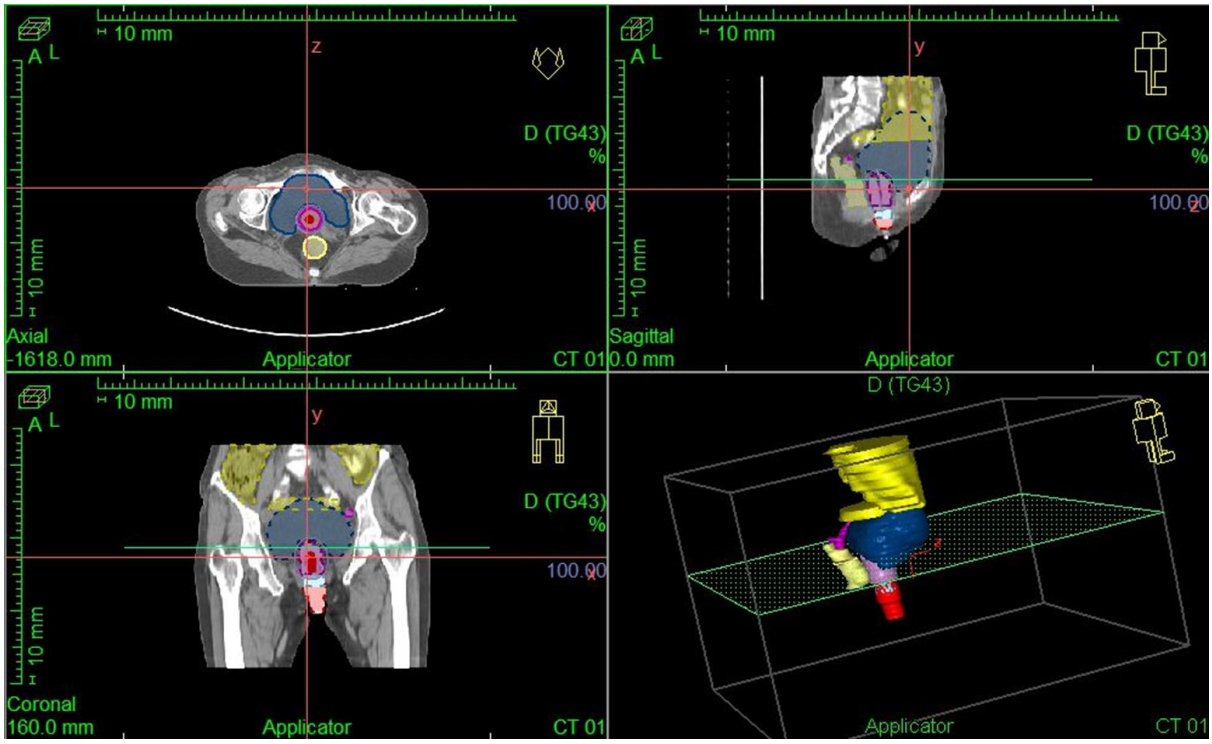



Fig13: Vaginal brachytherapy planning in Oncentra® Brachy Treatment Planning system

Two plans were created for each CT data set, one library based 2D plan and an optimised 3 D plan. Dose was prescribed to 5mm depth from the surface of the mould. Optimisation was done only in 3 D plan to minimise normal organ doses and to achieve best coverage possible (at least D95 >90%). Another plan was generated on the same CT using dwell positions and weightings from standard loaded library plans without any dose optimisation which was considered as a surrogate for 2D based plan. Dose

(%) to mould surface and 0.5cm depth was reported in terms of dose received by 90% of volume and 95% of volume (D90 & D95). Volume that received 100% dose and 150% dose (V100 & V150) at the mould surface and 0.5cm depth were also recorded. The organ at risk volume dose was be defined as dose (%) delivered to 0.1cc, 1cc, 2cc and 5cc of OAR (D0.1cc, D1cc, D2cc & D5cc).

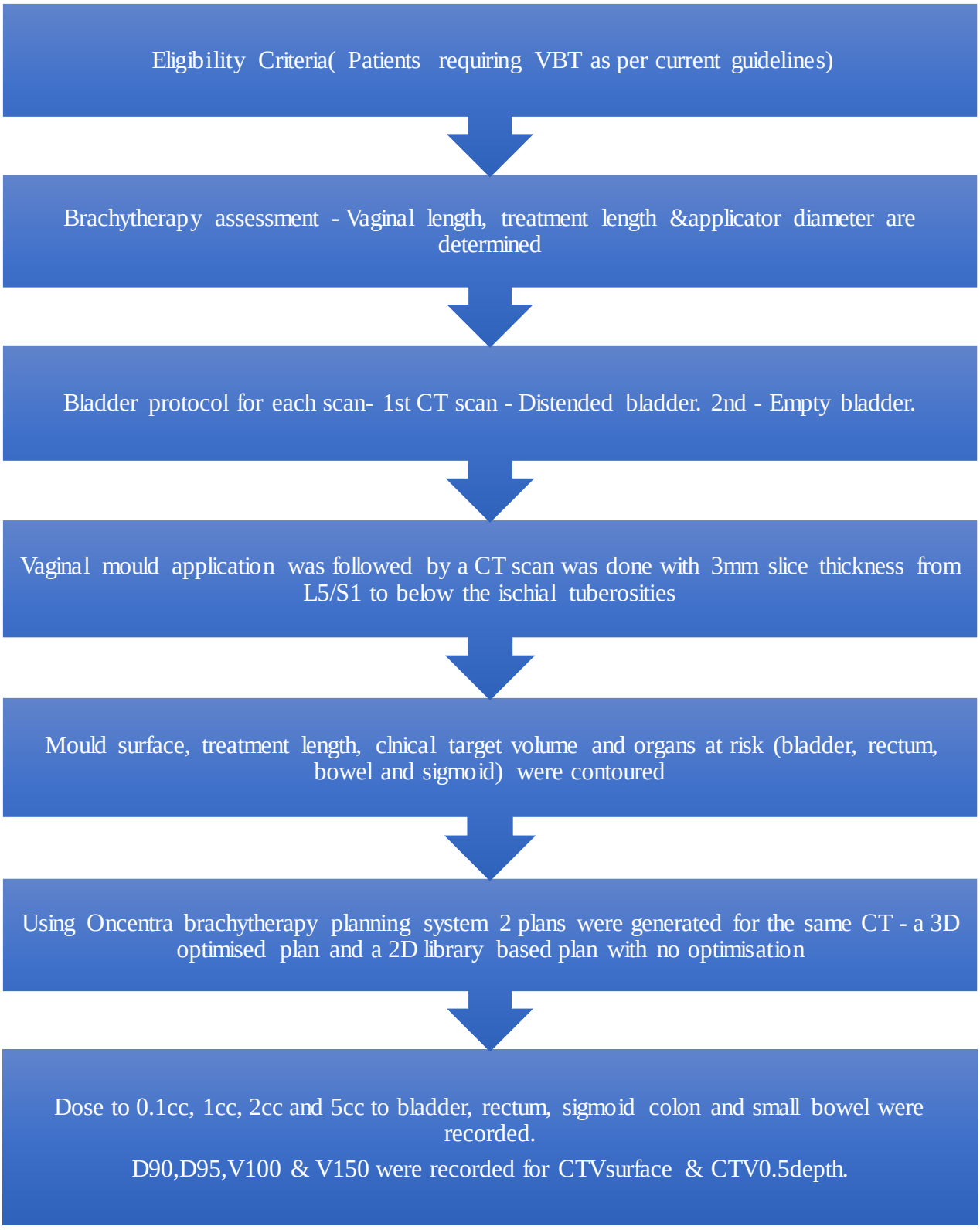
| ROI | Dose [%] | Dose [cGy] | Volume [%] | Volume [ccm] |
|---|---|---|---|---|
| ACTIVE LENGTH | | | | |
| ACTIVE LENGTH | 156.37 | - | **90.00** | 27.67 |
| ACTIVE LENGTH | 138.71 | - | **95.00** | 29.21 |
| BLADDER | | | | |
| BLADDER | 105.73 | - | 0.15 | **1.00** |
| BLADDER | 98.11 | - | 0.30 | **2.00** |
| BLADDER | 160.16 | - | 0.01 | **0.10** |
| BOWEL BAG1 | | | | |
| BOWEL BAG1 | 13.84 | - | 0.09 | **1.00** |
| BOWEL BAG1 | 13.01 | - | 0.19 | **2.00** |
| CTV 2D | | | | |
| CTV 2D | 100.23 | - | **90.00** | 54.25 |
| CTV 2D | 92.51 | - | **95.00** | 57.27 |
| RECTUM | | | | |
| RECTUM | 95.41 | - | 2.59 | **1.00** |
| RECTUM | 84.43 | - | 5.18 | **2.00** |
| SIGMOID | | | | |
| SIGMOID | 17.49 | - | 7.53 | **1.00** |
| SIGMOID | 15.73 | - | 15.07 | **2.00** |

Fig14: DVH parameters in vaginal brachytherapy planning

All dosimetric parameters described above were compared between the 3D based optimised plan and unoptimized library-based plan. The D2cc measurement had been determined to be representative of a clinically significant determinant of critical organ dosimetry in gynaecologic cancer by the Groupe European de Curie therapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO).(77–80)

As this was a dosimetric study, patients were treated with Ir-192 source from HDR nucletron® (Nucletron B.V., Netherlands) as per the conventional plan as it is the standard institutional practice. Plans generated for the study were not used for patient treatment.

## Detailed Diagrammatic Algorithm of The Study



## Statistical Analysis

For the sample size calculation, the statistical input of D2cc(% Dose to 2cc volume) Mean±SD of two organs at risk (bladder and rectum) for the conventional plan and CT based 3D plan was taken from the following reference article "Is there any advantage to three-dimensional planning for vaginal cuff brachytherapy? – Kim H et al "(76). The sample size was calculated using nMaster software version 2.0. Both plans were compared for each organ at risk (Rectum and Bladder) separately. The study required totally 92 observations to compare dose to target and organs at risk in conventional plan and CT based 3D plan in vaginal mould brachytherapy.

| **Single Mean - Paired t-test** | |
|---|---|
| Pre-test mean | **89.1** |
| Post-test mean | **85.1** |
| Standard deviation in Pre-test | **15** |
| Standard deviation in Post-test | **12.1** |
| Effect size | **0.295203** |
| Power (%) | **80** |
| Alpha Error | **5** |
| 1 or 2 sided | **2** |
| Required sample size | **92** |

**Formula**

$$N_{pairs} = \frac{\left(z_{1-\alpha/2} + z_{1-\beta}\right)^2}{\Delta^2} + \frac{z^2_{1-\alpha/2}}{2}$$

$$\Delta = \frac{(\mu_2 - \mu_1)}{\sigma} \qquad \sigma = \frac{\sigma_1 + \sigma_2}{2}$$

Where,

$\mu_1$ : Pre-test mean

$\mu_2$ : Post-test mean

$\sigma_1$ : Standard deviation in the pre-test

$\sigma_2$ : Standard deviation in the post-test

$\Delta$ : Effect size

$\alpha$ : Significance level

$1-\beta$ : Power

For continuous data such as age, the descriptive statistics n, Mean, SD, Median, IQR, range were presented. For categorical data, the number of patients and percentage were presented. The Shapiro–Wilk and Kolmogorov–Smirnov tests were used to test the hypothesis of normal distribution. Based on the normality of data, the parametric paired t test or non-parametric Wilcoxon signed rank test were applied to the data. P-values were reported as specified by the statistical software used, at least up to four decimal places. P-values less than 0.0001 were reported as provided by statistical software (e.g. '<0.0001'). All tests were two-sided at $\alpha$=0.05 level of significance. All analyses were done using Statistical Package for Social Services (SPSS) software Version 21.0 (Armonk, NY: IBM Corp).

## RESULTS

43 patients were enrolled in the study and 92 observations (Planning CTs) were made. Their median age was 49 years (Range – 24 – 69). All patients had undergone hysterectomy and 54% (n = 23) of patients were diagnosed with carcinoma endometrium, followed by carcinoma cervix (30%) and carcinoma cervical stump (16%). [Fig 15]

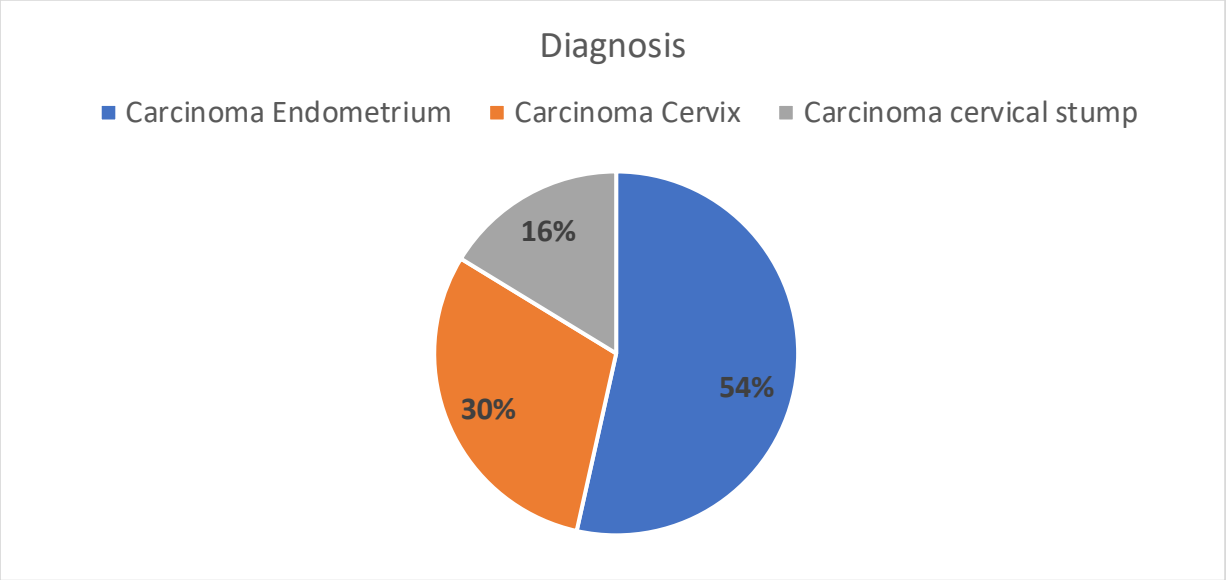



Figure 15: Diagnosis

## External beam radiation therapy:

All patients recruited in this study had risk factors with indications for adjuvant radiation therapy of which 86% (n = 37) received external beam radiation prior to vaginal brachytherapy and 14% (n = 6) had vaginal brachytherapy alone.

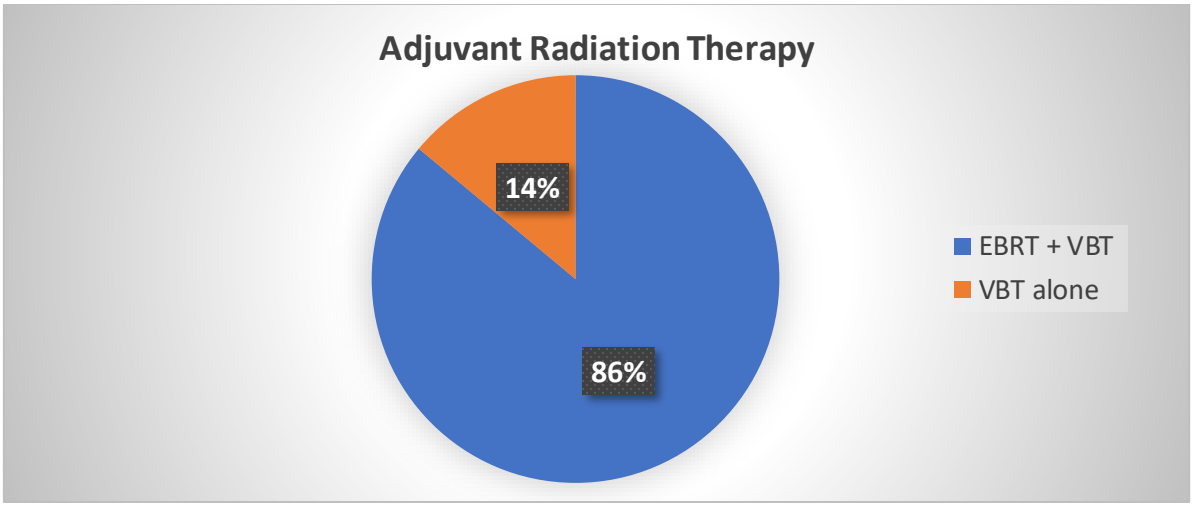



Figure 16: Adjuvant radiation therapy

Of the patients who underwent external beam radiation therapy, 68% had intensity modulated radiation therapy (IMRT)/Volumetric modulated arc technique (VMAT), 16% underwent 3DCRT and 16% underwent conventional 2D technique using Cobalt 60 or Linac [Fig 17 & 18].

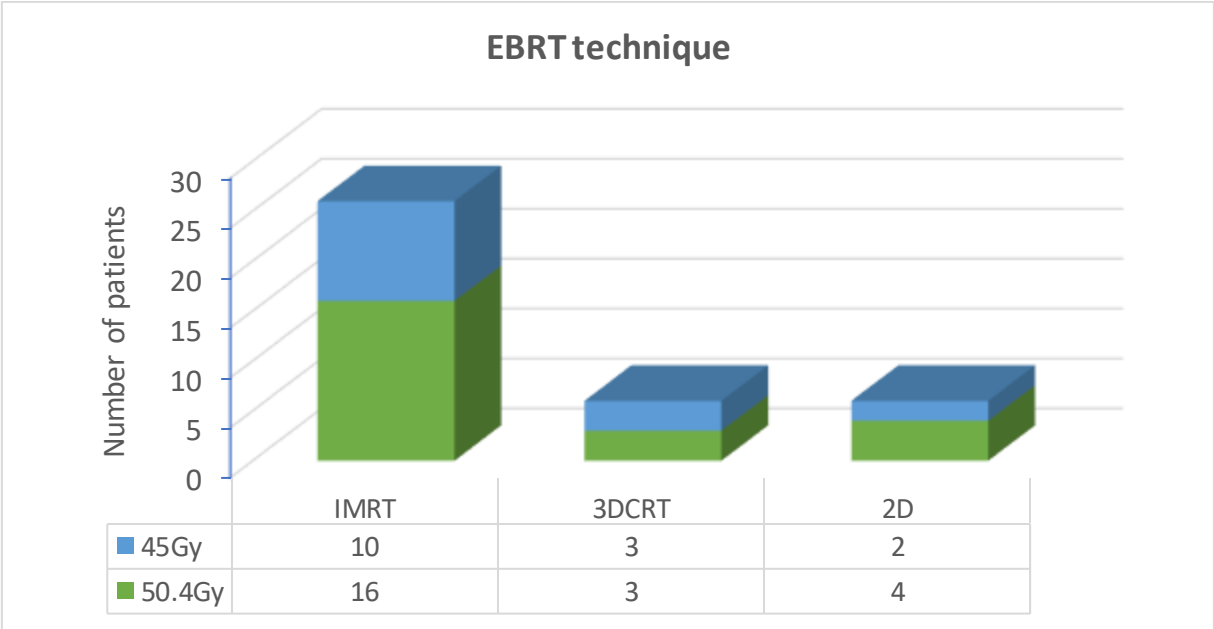



Figure 17: External beam radiation therapy technique

All patients who underwent IMRT/VMAT and 3DCRT did not have any acute grade II/III gastrointestinal or genitourinary toxicity. 3 patients who underwent treatment with conventional Cobalt 60 developed grade II diarrhoea and 2 patients required breaks in radiation therapy.

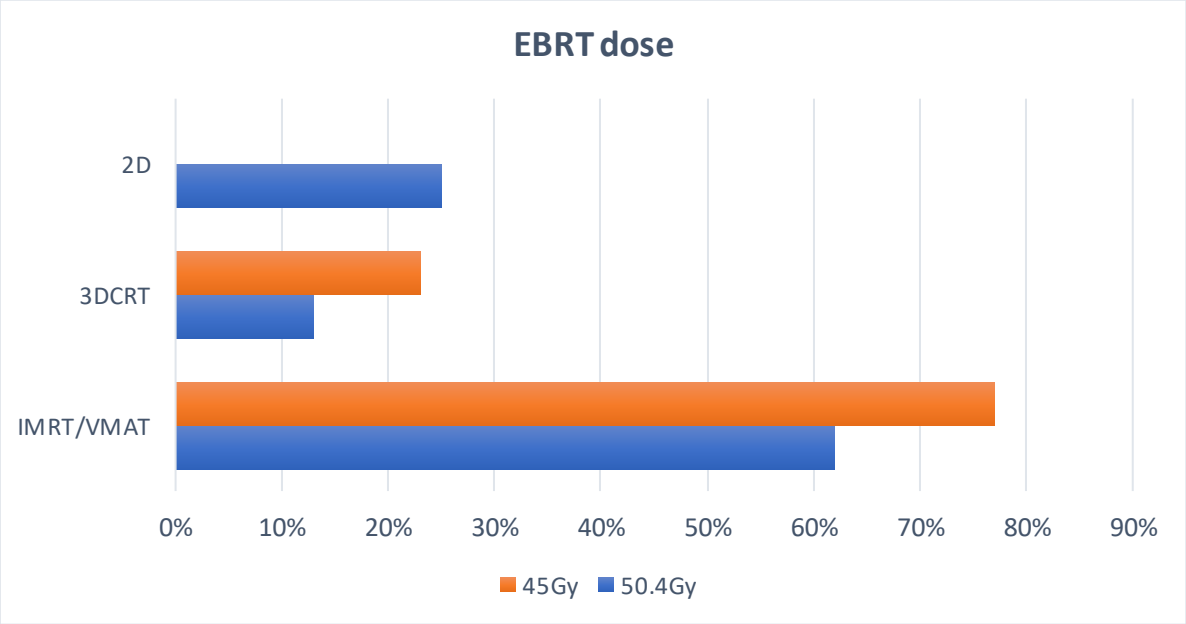



Figure 18: External beam radiation therapy dose

## Vaginal mould brachytherapy

All patients were assessed prior to vaginal brachytherapy and vaginal length and diameter were determined. 70% (n = 30) of the patients required a 3cm diameter cylinder and 30% (n=13) required a 2.5cm diameter vaginal cylinder. Treatment length was determined as 2/3$^{rd}$ of total vaginal length based on clinical assessment and correlated with vaginal length on planning CT. Median treatment length was 4.5 cm (range – 4 – 5 cm). Planning CTs were done with full and empty bladder

protocols. Initial 6 patients underwent a 3rd CT which was taken with bladder in a variable state of filling determined by patient's choice and comfort.

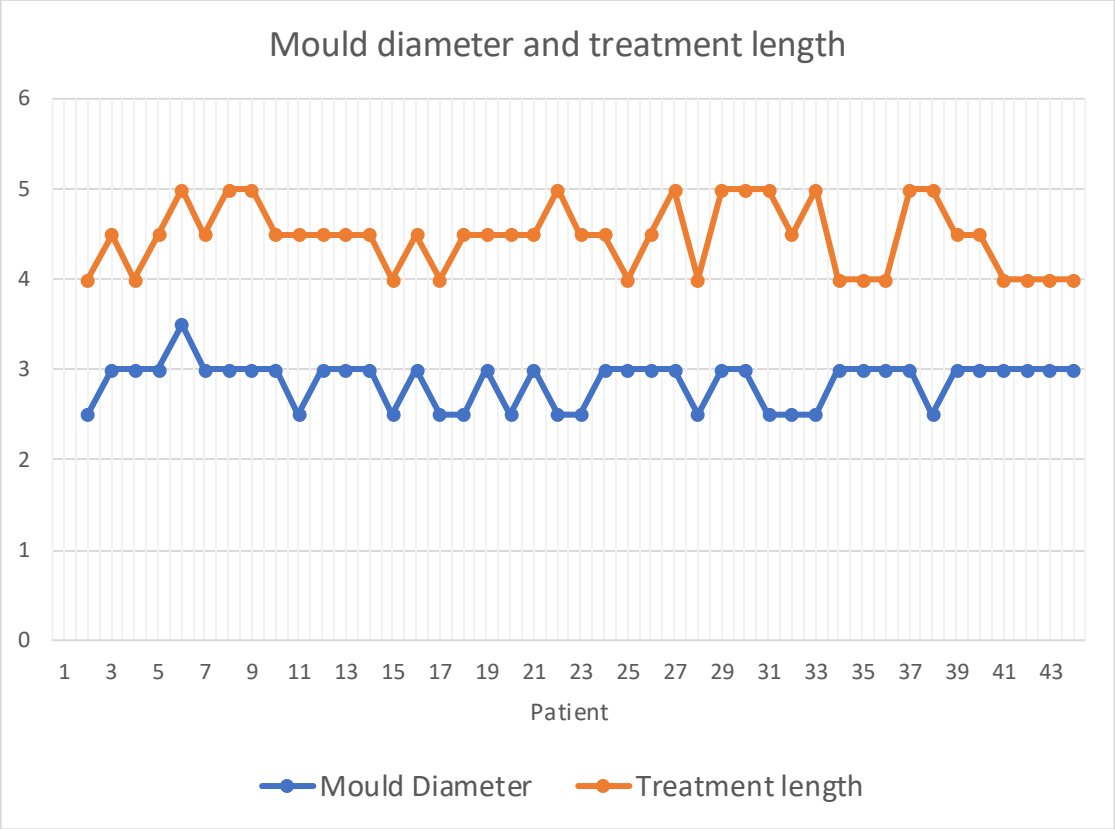



Fig:19 : Vaginal cylinder diameter and treatment length

## Target volume dosimetry – 2D Vs 3D

Dose was prescribed to 5mm depth from the surface of the mould. Mean CTVsurface volume was 28.8cc (range 18.6cc– 39cc) and mean CTVdepth volume was 53cc (range 36.3cc – 68cc). The mean percentage of CTV that was encompassed by the prescribed dose (V100) in 2D based unoptimized planning was 99.71% (range – 88.46% - 100%) for

CTVsurface and 89.54% (range 77.9% - 99.7%) for CTVdepth. The mean percentage of CTV volume that was encompassed by the prescribed dose (V100) in 3D based optimized planning was 99.54% (range 93.36% - 100%) for CTVsurface and 87.17% (range – 75.17% - 93.78%) for CTVdepth [Table 4 & 5]. Difference between CTV coverage in terms of optimised and non-optimised plans were not statistically significant for CTVsurface (p=0.286) and CTVdepth (p=0.11).

| | **CTVsurface** | | | |
|---|---|---|---|---|
| | **2D** | | **3D** | |
| | Mean | SD | Mean | SD |
| **V100** | 99.71 | 1.22 | 99.54 | 1.04 |
| **V150** | 92 | 4.19 | 85.9 | 4.52 |
| **D95** | 143 | 12.48 | 133 | 6.9 |
| **D90** | 157 | 11.7 | 143.42 | 7.09 |

Table 4: DVH parameters for CTVsurface in 2D and 3D plans

Mean percentage of prescription dose to 95% of CTVdepth (D95%) was 92.8% (range – 82.7% – 117.36%) for unoptimized plan and 89.75% (range – 82.96% – 98.41%) optimised plan. Mean percentage of

prescription dose to 90% of CTVdepth (D90%) was 100.2% (range – 89% – 124.57%) for unoptimized plan and 96.9% (range – 90% – 105.27%) optimised plan. All but 17 plans in both groups had D90 less than 100% and none of the plans in 3D group had D90 less than 90% of the prescribed dose. Wilcoxon signed ranks test were performed and no statistical difference was observed between D90 and D95 of CTVdepth in 2D and 3D based planning [Fig 20].

| | **CTVdepth** | | | |
|---|---|---|---|---|
| | **2D** | | **3D** | |
| | Mean | SD | Mean | SD |
| **V100** | 89.5 | 4.29 | 87.17 | 3.14 |
| **V150** | 52.4 | 5.3 | 50.33 | 3.11 |
| **D95** | 92.8 | 6.68 | 89.75 | 3.11 |
| **D90** | 100.2 | 6.62 | 96.9 | 3.23 |

Table 5: DVH parameters for CTVdepth in 2D and 3D plans

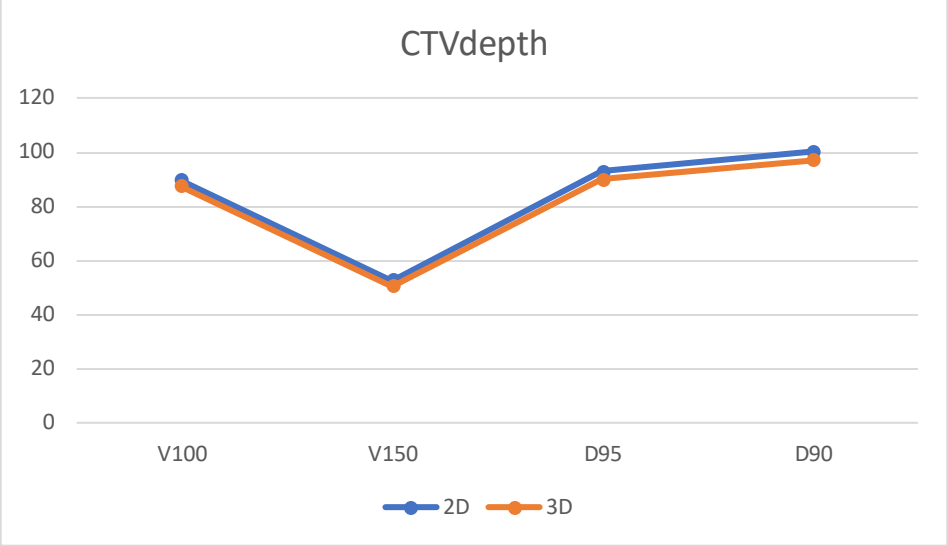



Fig 20: Comparison of 2D and 3D dose parameters in CTV depth

## Organs at risk dosimetry – 2D Vs 3D

### Bladder

Mean bladder volume in 92 observations was 216cc (Range 33 – 669.5 cc). The mean D0.1cc, D1cc, D2cc and D5cc for 2D Vs 3D based plans were 107.33% Vs 87.8% (p = <0.001), 86.6% Vs 72.03% (p = <0.001), 78.85% Vs 65.9% (p = <0.001) and 65.92% Vs 55.3% ( p = <0.001) respectively [Table 6, Fig 21]. On further analysis, it was observed that D2cc was >100% in 11 (12%) patients with 2D based plan and only 1 patient had D2cc >100% in the 3 D based plan.

| Parameter (Bladder) | | Mean (%) | SD | Paired Samples test | | | |
|---|---|---|---|---|---|---|---|
| | | | | Correlation | 95% CI | | P value (2 tailed) |
| | | | | | Lower | Upper | |
| **D0.1cc** | 2D | 107.33 | 29.21 | 0.904 | 16.73 | 22.32 | <0.001 |
| | 3D | 87.80 | 21.30 | | | | |
| **D1cc** | 2D | 86.65 | 20.42 | 0.927 | 12.933 | 16.30 | <0.001 |
| | 3D | 72.03 | 16.16 | | | | |
| **D2cc** | 2D | 78.85 | 18.58 | 0.939 | 11.48 | 14.35 | <0.001 |
| | 3D | 65.92 | 14.82 | | | | |
| **D5cc** | 2D | 65.92 | 16.59 | 0.946 | 9.414 | 11.81 | <0.001 |
| | 3D | 55.31 | 13.5 | | | | |

Table 6: DVH parameters for bladder in 2D and 3D plans

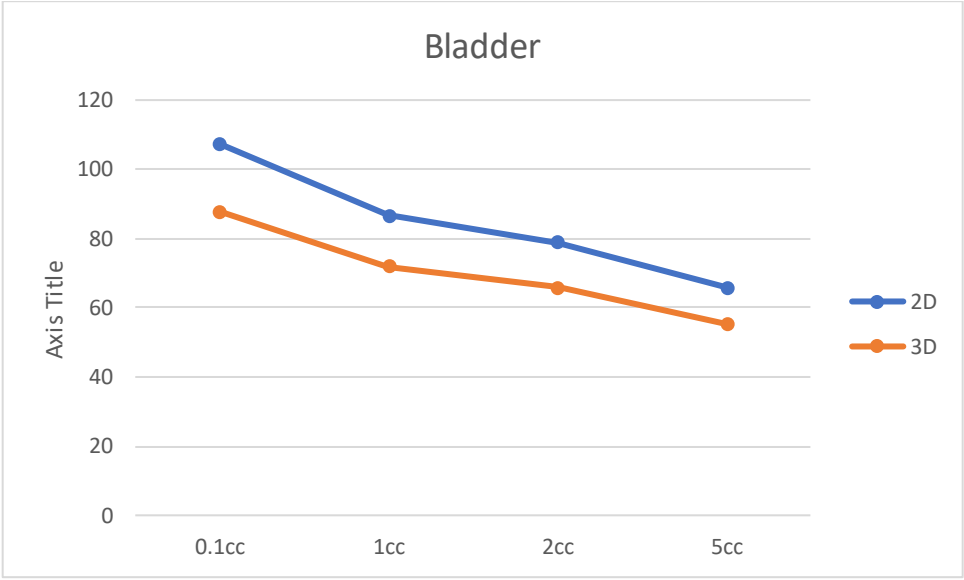



Fig 21: Comparison of 2D and 3D dose parameters in bladder

## Rectum

Mean rectum volume in 92 observations was 46cc (Range 33 – 669.5 cc). The mean D0.1cc, D1cc, D2cc and D5cc for 2D Vs 3D based plans were 115.65% Vs 93.93% (p = <0.001), 90.68% Vs 76.12% (p = <0.001), 80.19% Vs 67.24% (p =

0.033) and 62.88% Vs 53.17% ( p = 0.086) respectively [Table 7, Fig 22]. On further analysis, it was observed that D2cc to rectum was >100% in 16 (17%) plans with 2D based planning and no plans had D2cc >100% with the 3D based optimised planning. Only one 3D plan had rectal D2cc >90% as opposed to 25 plans (27%) done based on 2D based planning.

| Parameter (Rectum) | | Mean (%) | SD | Paired Samples test | | | |
|---|---|---|---|---|---|---|---|
| | | | | Correlation | 95% CI | | P value (2 tailed) |
| | | | | | Lower | Upper | |
| **D0.1cc** | 2D | 115.65 | 25.41 | 0.668 | 17.71 | 25.72 | <0.001 |
| | 3D | 93.93 | 12.94 | | | | |
| **D1cc** | 2D | 90.68 | 17.36 | 0.866 | 12.66 | 16.46 | <0.001 |
| | 3D | 76.12 | 12.04 | | | | |
| **D2cc** | 2D | 80.19 | 16.39 | 0.784 | 10.84 | 15.05 | 0.033 |
| | 3D | 67.24 | 12.65 | | | | |
| **D5cc** | 2D | 62.88 | 15.18 | 0.937 | 8.47 | 10.94 | 0.086 |
| | 3D | 53.17 | 11.52 | | | | |

Table 7: DVH parameters for rectum in 2D and 3D plans

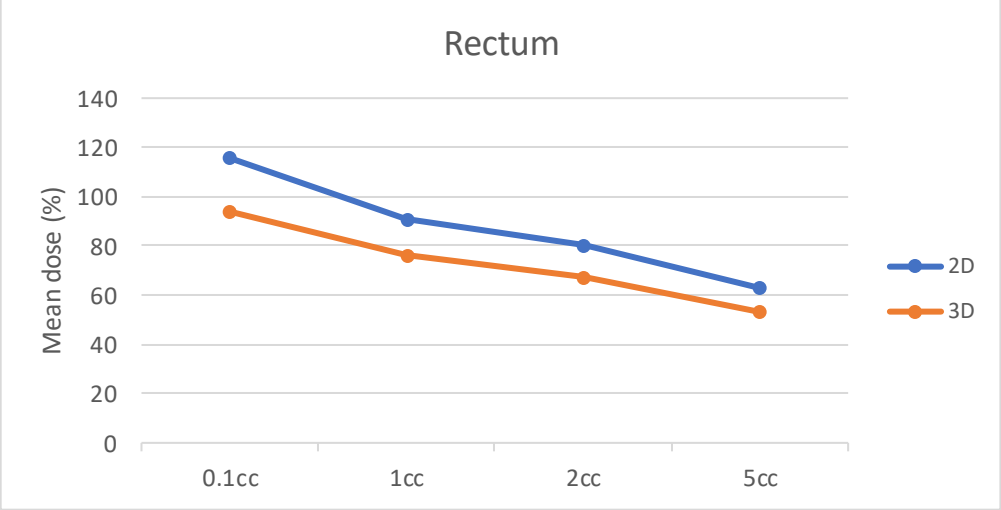



Fig 22: Comparison of 2D and 3D dose parameters in Rectum

## Sigmoid colon

Mean sigmoid colon volume in 92 observations were 34 cc (Range 11.7 – 125 cc). The mean D0.1cc, D1cc, D2cc and D5cc for 2D Vs 3D based plans were 29.09% Vs 24.15% (p = <0.001), 23.07% Vs 19.12% (p = <0.001), 20.74% Vs 17.15% (p = 0.022) and 16.98% Vs 14.12% (p = 0.035) respectively [Table 8, Fig 23]. On further analysis, it was observed that D2cc to sigmoid colon was >50% in 2 (1%) and >30% in 17 (18%) plans with 2D based planning and no plans had D2cc of sigmoid colon was >50% and >30% was 10 (11%) plans with the 3D based optimised planning. The maximum point dose (D0.1cc) was 90.95% with 2D based plan whereas 72.15% with the 3D based plan.

| Parameter (Sigmoid) | | Mean (%) | SD | Wilcoxon Signed Ranks Test | |
|---|---|---|---|---|---|
| | | | | Z | p value (2 tailed) |
| **D0.1cc** | 2D | 29.09 | 18.02 | -8.002 | <0.001 |
| | 3D | 24.15 | 13.74 | | |
| **D1cc** | 2D | 23.07 | 13.53 | -7.953 | <0.001 |
| | 3D | 19.12 | 10.49 | | |
| **D2cc** | 2D | 20.74 | 11.7 | -7.971 | 0.022 |
| | 3D | 17.15 | 9.18 | | |
| **D5cc** | 2D | 16.98 | 9.17 | -7.940 | 0.035 |
| | 3D | 14.12 | 7.25 | | |

Table 8: DVH parameters for sigmoid in 2D and 3D plans

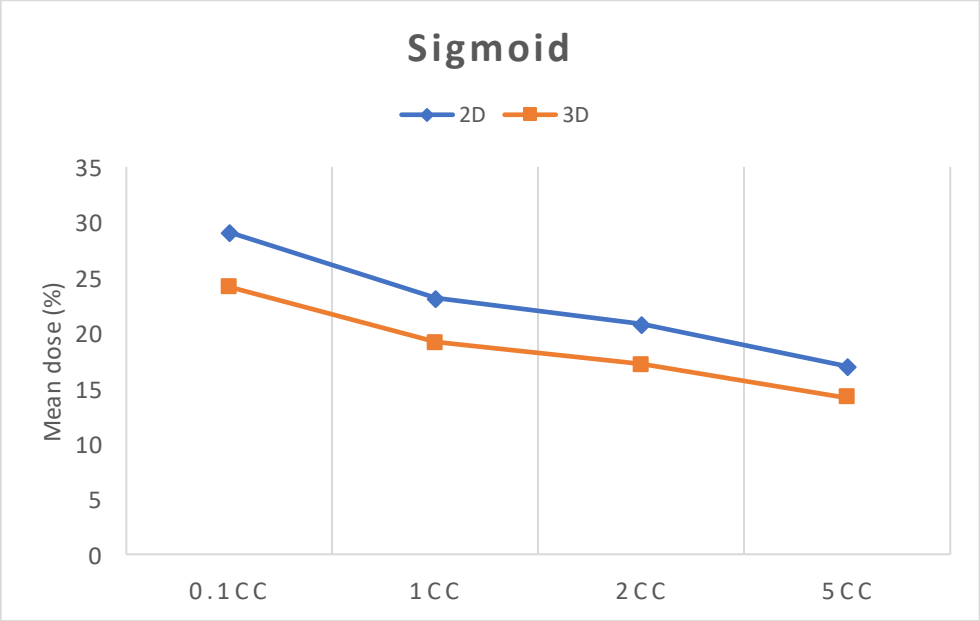



Fig 23: Comparison of 2D and 3D dose parameters in CTVdepth

## Bowel

Mean bowel volume was 460 cc (Range 85.2 – 854.9 cc). The mean D0.1cc, D1cc, D2cc and D5cc for 2D Vs 3D based plans were 38.44% Vs 31.4% (p = <0.001), 31.24% Vs 25.24% (p = <0.001), 28.25% Vs 22.84% (p = <0.001) and 23.66% Vs 19.48% (p = <0.001) respectively [Table 9, Fig 24]. The maximum

point dose (D0.1cc) was 114.76% with 2D based plan whereas 101.7% with the 3D based plan. On further analysis, it was observed that D2cc to bowel was >50% in 19 (20%) plans and >30% of prescribed dose in 34 (37%) plans with 2D based planning and D2cc of bowel was >50% in only 7 (8%) plans and >30% was 25 (26%) plans with the 3D based optimised planning. Dose to bowel can be significantly reduced with 3D based optimisation.

| Parameter (Bowel) | | Mean (%) | SD | Wilcoxon Signed Ranks Test | |
|---|---|---|---|---|---|
| | | | | Z | p value (2 tailed) |
| **D0.1cc** | 2D | 38.44 | 29.90 | -7.817 | <0.001 |
| | 3D | 31.4 | 22.08 | | |
| **D1cc** | 2D | 31.24 | 24.86 | -7.837 | <0.001 |
| | 3D | 25.24 | 17.95 | | |
| **D2cc** | 2D | 28.25 | 21.92 | -7.871 | <0.001 |
| | 3D | 22.84 | 15.95 | | |
| **D5cc** | 2D | 23.66 | 17.80 | -7.663 | <0.001 |
| | 3D | 19.48 | 13.29 | | |

Table 9: DVH parameters for bowel in 2D and 3D plans

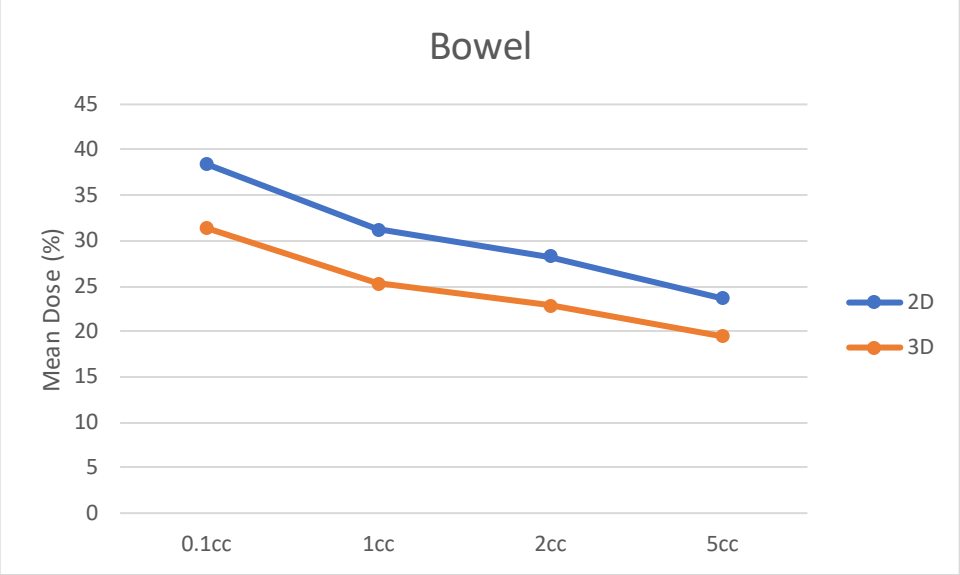



Fig 24: Comparison of 2D and 3D dose parameters in Bowel

## Effect of bladder filling

The mean volume of full bladder is 368cc (Range180.4cc – 669.5cc) and mean volume of empty bladder was 70cc (Range: 23cc – 173cc).

## Effect on target volumes

The effect of full bladder and empty bladder on target volumes CTVsurface and CTVdepth were analysed. None of the differences in the parameters of 2D and 3D based plans were statistically significant neither for CTVsurface nor CTVdepth [Table 10 & 11].

| Variables | | Full Bladder (n=46) | | Empty bladder (n=46) | | Mean Difference | 95% Confidence Interval of the Difference | | p value |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | | Lower | Upper | |
| **2D CTVsurface** | D90 | 159.44 | 12.53 | 155.80 | 10.69 | 3.64 | -1.19 | 8.46 | .138 |
| | D95 | 145.83 | 12.73 | 141.39 | 11.97 | 4.43 | -0.68 | 9.55 | .089 |
| | V100 | 99.60 | 1.71 | 99.82 | 0.32 | -0.22 | -0.73 | 0.29 | .386 |
| | V150 | 92.69 | 4.68 | 91.81 | 3.66 | 0.89 | -0.85 | 2.62 | .315 |
| **3D CTVsurface** | D90 | 144.15 | 7.60 | 142.70 | 6.55 | 1.45 | -1.49 | 4.39 | .330 |
| | D95 | 133.77 | 6.96 | 132.31 | 6.84 | 1.45 | -1.40 | 4.31 | .315 |
| | V100 | 99.42 | 1.36 | 99.67 | 0.55 | -0.25 | -0.68 | 0.18 | .253 |
| | V150 | 86.38 | 5.15 | 85.60 | 3.83 | 0.77 | -1.11 | 2.66 | .415 |

Table 10: Comparison of dose parameters in full and empty bladder state for CTVsurface

| Variables | | Full Bladder (n=46) | | Empty bladder (n=46) | | Mean Difference | 95% Confidence Interval | | p value |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | | Lower | Upper | |
| **2D CTVdepth** | D90 | 101.00 | 6.70 | 99.43 | 6.52 | 1.57 | -1.17 | 4.30 | .259 |
| | D95 | 93.70 | 6.67 | 91.91 | 6.66 | 1.79 | -0.97 | 4.55 | .202 |
| | V100 | 90.11 | 4.09 | 88.98 | 4.46 | 1.13 | -0.65 | 2.90 | .210 |
| | V150 | 53.08 | 5.41 | 51.74 | 5.17 | 1.34 | -0.85 | 3.54 | .227 |
| **3D CTVdepth** | D90 | 96.99 | 3.19 | 96.88 | 3.31 | 0.11 | -1.23 | 1.46 | .868 |
| | D95 | 89.60 | 3.21 | 89.92 | 3.05 | -0.32 | -1.62 | 0.97 | .621 |
| | V100 | 87.22 | 3.10 | 87.13 | 3.22 | 0.09 | -1.22 | 1.40 | .895 |
| | V150 | 50.44 | 3.44 | 50.22 | 2.78 | 0.23 | -1.07 | 1.52 | .731 |

Table 11: Comparison of dose parameters in full and empty bladder state for CTVdepth

## Effect on organs at risk

All the organs at risk parameters were compared in full and empty bladder states. D2cc and D5cc of bladder showed statistically significant reduction in bladder dose in empty state (Volume <180cc) as compared to full state [Table 12]. Rectum and sigmoid parametric differences with

respect to bladder filling was not statistically significant [Table 13&14 ]. Bladder distension was observed to significantly reduce the dose to bowel and the differences were statistically significant ($p < 0.001$) [Table 15].

Bladder

| Variables (Bladder) | | Full Bladder (n=46) | | Empty bladder (n=46) | | Mean Difference | 95% Confidence Interval | | p value |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | | Lower | Upper | |
| **2D** | D90 | 111.77 | 31.18 | 102.90 | 26.71 | 8.88 | -3.15 | 20.90 | .146 |
| | D95 | 90.48 | 21.23 | 82.83 | 19.05 | 7.64 | -0.71 | 16.00 | .073 |
| | V100 | 82.94 | 19.41 | 74.77 | 16.96 | 8.17 | 0.61 | 15.72 | **.034** |
| | V150 | 71.16 | 17.67 | 60.70 | 13.74 | 10.46 | 3.90 | 17.01 | **.002** |
| **3D** | D90 | 90.22 | 23.06 | 85.39 | 19.35 | 4.83 | -3.99 | 13.65 | .279 |
| | D95 | 74.70 | 17.21 | 69.37 | 14.75 | 5.33 | -1.31 | 11.97 | .114 |
| | V100 | 68.99 | 15.88 | 62.87 | 13.16 | 6.12 | 0.07 | 12.16 | **.047** |
| | V150 | 59.79 | 13.98 | 50.84 | 11.52 | 8.95 | 3.65 | 14.26 | **.001** |

Table 12: Comparison of dose parameters in full and empty bladder state for Bladder

Rectum

| Variables (Rectum) | | Full Bladder (n=46) | | Empty bladder (n=46) | | Mean Difference | 95% Confidence Interval | | p value |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | | Lower | Upper | |
| 2D | D90 | 117.80 | 27.44 | 113.51 | 23.32 | 4.29 | -6.26 | 14.84 | .422 |
| | D95 | 91.05 | 17.31 | 90.32 | 17.60 | 0.73 | -6.50 | 7.96 | .841 |
| | V100 | 80.50 | 16.43 | 79.88 | 16.53 | 0.62 | -6.20 | 7.45 | .857 |
| | V150 | 63.38 | 15.32 | 62.38 | 15.20 | 1.00 | -5.32 | 7.32 | .754 |
| 3D | D90 | 94.66 | 13.57 | 93.21 | 12.40 | 1.45 | -3.93 | 6.84 | .593 |
| | D95 | 76.64 | 12.63 | 75.60 | 11.56 | 1.04 | -3.97 | 6.06 | .681 |
| | V100 | 66.99 | 13.68 | 67.49 | 11.68 | -0.50 | -5.77 | 4.77 | .852 |
| | V150 | 53.70 | 11.80 | 52.65 | 11.36 | 1.05 | -3.75 | 5.84 | .666 |

Table 13: Comparison of dose parameters in full and empty bladder state for Rectum

## Sigmoid

| Variables (Sigmoid) | | Full Bladder (n=46) | | Empty bladder (n=46) | | Mean Difference | 95% Confidence Interval of the Difference | | p value |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | | Lower | Upper | |
| **2D** | D90 | 26.37 | 17.07 | 31.82 | 18.91 | -5.45 | -12.92 | 2.01 | .150 |
| | D95 | 20.94 | 12.81 | 25.21 | 14.18 | -4.27 | -9.87 | 1.33 | .133 |
| | V100 | 18.80 | 10.97 | 22.68 | 12.33 | -3.87 | -8.71 | 0.96 | .115 |
| | V150 | 15.29 | 8.53 | 18.68 | 9.66 | -3.40 | -7.17 | 0.38 | .077 |
| **3D** | D90 | 21.83 | 13.02 | 26.47 | 14.34 | -4.64 | -10.31 | 1.04 | .108 |
| | D95 | 17.20 | 9.95 | 21.05 | 10.89 | -3.85 | -8.17 | 0.47 | .080 |
| | V100 | 15.44 | 8.75 | 18.87 | 9.49 | -3.43 | -7.21 | 0.35 | .075 |
| | V150 | 12.64 | 7.02 | 15.62 | 7.33 | -2.98 | -5.96 | -0.01 | .050 |

Table 14: Comparison of dose parameters in full and empty bladder state for Sigmoid

## Bowel

| Variables (Bowel) | | Full Bladder (n=46) | | Empty bladder (n=46) | | Mean Difference | 95% Confidence Interval of the Difference | | p value |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | | Lower | Upper | |
| **2D** | D90 | 20.49 | 12.28 | 56.40 | 31.91 | -35.91 | -46.00 | -25.82 | **<0.001** |
| | D95 | 16.20 | 10.20 | 46.29 | 26.40 | -30.09 | -38.44 | -21.74 | **<0.001** |
| | V100 | 14.93 | 9.24 | 41.58 | 23.12 | -26.65 | -33.99 | -19.30 | **<0.001** |
| | V150 | 12.64 | 7.54 | 34.70 | 18.51 | -22.07 | -27.96 | -16.17 | **<0.001** |
| **3D** | D90 | 17.87 | 7.75 | 45.00 | 23.68 | -27.13 | -34.49 | -19.77 | **<0.001** |
| | D95 | 14.05 | 6.98 | 36.43 | 18.82 | -22.38 | -28.31 | -16.46 | **<0.001** |
| | V100 | 12.82 | 6.44 | 32.88 | 16.53 | -20.06 | -25.29 | -14.82 | **<0.001** |
| | V150 | 11.07 | 5.57 | 27.90 | 13.63 | -16.83 | -21.17 | -12.49 | **<0.001** |

Table 15: Comparison of dose parameters in full and empty bladder state for bowel

In full bladder state, 8.33% (p = 0.04) increase in bladder dose was noted. But the mean dose (D50%) to bladder was observed to be reduced by 13.7% in full bladder state. A statistically insignificant 1.21% increase in rectum dose was noted in full bladder state. An 4% mean reduction in sigmoid dose was noted in full bladder state but it was statistically insignificant marginally (p = 0.068). A 35% reduction in bowel dose was noted which was statistically significant (p =<0.001). [Fig 25]

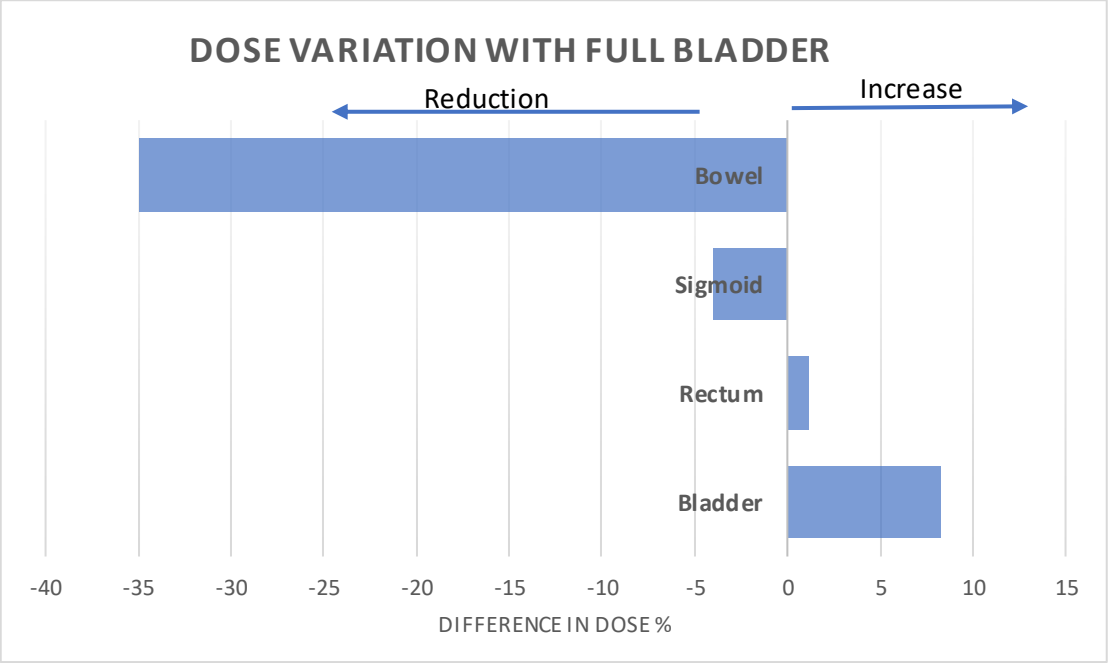



Fig 25: Dose variation in organs at risk in full bladder state

# DISCUSSION

Vaginal cuff HDR brachytherapy is commonly used in the treatment for carcinoma of the endometrium, cervix and vagina. Despite significant technological advances in medical imaging, external beam radiation therapy planning and delivery techniques, few developments have occurred with vaginal cuff brachytherapy over the years. According to 2014 ABS survey, although wide variation among practitioners exist with respect to dose/fractionation and treatment length. The most commonly used applicators to deliver vaginal brachytherapy is vaginal cylinders and single channel applicator being the commonest.(75) Although many centers have CTs simulators, cross sectional imaging is often used only to confirm applicator placement and library plans are used for treatment. One of the reasons why 3D volume-based planning has not been used in vaginal brachytherapy is that the published outcome data with conventional planning is excellent (68,70,81,82). The primary aim of the study was to evaluate if transition from 2D to 3D based planning would make a significant difference dosimetrically. Secondary aim was to analyse the effect of bladder distension on target volume and normal tissue dosimetry. As there is a paucity of large data experience in the literature and lack of consensus guidelines for vaginal cuff brachytherapy, this study was undertaken.

In this study, the variation in target volume dosimetry to cylinder surface and at 0.5cm depth in 2D and 3D based plans were observed to be minimal and not statistically significant. This was consistent with study by Kim et al(76), where the CTV parameters of 2D and 3D based planning did not have significant difference. In a study by Holloway et al (83) evaluating 3D dosimetry for vaginal brachytherapy, it was reported that re-planning for each fraction did not make any significant difference in dosimetry. With respect to target volume dosimetry, the same was observed in our study.

Previously published data (84–87) on cervical cancers with an intact uterus have suggested that ICRU reference points doses may not correlate well with dose to D2cc of bladder which, according to GEC-ESTRO guidelines, is considered to more accurate in predicting toxicity outcomes. With image-based brachytherapy, apart from applicator placement and treatment length, OAR volumetric dosimetry can be determined. With 3D based planning, dose optimisation is done to minimise the OAR doses within acceptable limits. More so ever, patients who had undergone conformal external beam radiation therapy, cumulative EQD2 can be accurately calculated and thus help in reducing toxicities.

Although the presence of uterus in treatment of cervical cancer provides additional protection to small bowel, studies investigating intracavitary

brachytherapy with tandem and ovoids have showed significant reduction in bowel dose with distended bladder. As small bowel is more radiosensitive and has lesser radiation tolerance threshold, treatment with full bladder will be more beneficial in decreasing hot spot to the small bowel. In our study, 35% reduction in bowel dose was observed in full bladder state with a marginal increase in D2cc bladder doses and non-significant decrease in mean bladder dose (D50%). Similarly, in a study by Hung et al(88), dosimetric advantage to the small bowel with distended bladder was accompanied by a non-significant increase in D2cc but a significant decrease in mean dose to bladder (D50%). In a distended state, posterior wall of bladder is in close proximity to the brachytherapy applicator and hence, the dose is increased significantly. In addition to this, posterolateral wall of the full bladder bulge on the either side of vaginal cuff to form the 'bladder horns' around the high dose region which contributes to high D2cc of bladder dose.

There have been few similar studies which examined effect of bladder filling on normal organs in post hysterectomy patients(79,89). Hoskin et al(79) evaluated the effect of bladder volume on normal organ dosimetry by using various volumes of such as 35, 70 or 100ml of bladder filling by instillation using a Foley's catheter. They evaluated dose via 2D measurements of bladder height and measured the volume of small bowel

within the high dose region. In their study, they found 57.5% reduction in small bowel volume within the high dose region and concluded that vaginal brachytherapy should be administered with at least 100 ml of bladder filling. Volumetric parameters of bladder and dose to bowel and sigmoid were not assessed. However, their findings regarding reduction in small bowel area in high dose region was consistent with the findings in our study. In our study, we observed a 35% reduction the bowel dose in distended bladder state.

In our study , the dose to sigmoid did not have significant reduction (8%, p =0.098) as compared to a study published by Hollway et al(83) which showed 20.3% reduction. This is likely because of interfraction variation of mobility of sigmoid and often it lies posterior to the bladder which make it less likely to be pushed away from the applicator by a distended bladder.

However, there were certain limitations of this study. Firstly, as this study was undertaken as a dosimetric study, clinical implications of our findings could not be demonstrated. A prospective study with long term follow-up is required for demonstrating if the dosimetric advantage is translated to clinical benefit. Furthermore, normal organ contouring on planning CT was based on RTOG normal organ contouring guidelines which is not specific for brachytherapy contouring and contouring of OARs were

subject to interpretation. To minimize variation and for standard volumes, all contouring was done by the primary investigator. Despite a strict bladder protocol, a wide variation in bladder filling was noted in terms of empty and full bladder. Urinary catheter use for bladder filling and emptying was discontinued due to patient discomfort. Finally, rectal distension and its effect on rectal dosimetry was not assessed in this study.

In spite of the limitations enlisted, this study aided us to elucidate the dosimetric advantages of image-based 3D vaginal vault brachytherapy as compared to conventional standard loading technique and also, we were able to develop an institution-based protocol for 3D Imaged guided Vault Brachytherapy as annexed [Annexure A].

# CONCLUSION

Our study established the dosimetric benefits with CT based 3D planning for vaginal brachytherapy over 2D based conventional planning. 3D CT based planning helps to decrease dose to critical organs without compromising target volume coverage by individualising the dosimetry according to each patient's anatomy. This study also illustrated the dosimetric benefit of bladder distension in lowering small bowel doses and aided us to develop an institutional protocol for image-based vault brachytherapy. As a result of this study, an effective transition from 2D based conventional planning to a 3D imaged based optimised vaginal brachytherapy planning could be achieved at our institution. The long term toxicity outcomes will further validate the benefits see in this dosimetric study.

# REFERENCES


1. Sedlis A, Bundy BN, Rotman MZ, Lentz SS, Muderspach LI, Zaino RJ. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A Gynecologic Oncology Group Study. Gynecol Oncol. 1999 May;73(2):177–83.

2. Rotman M, Sedlis A, Piedmonte MR, Bundy B, Lentz SS, Muderspach LI, et al. A phase III randomized trial of postoperative pelvic irradiation in Stage IB cervical carcinoma with poor prognostic features: follow-up of a gynecologic oncology group study. Int J Radiat Oncol Biol Phys. 2006 May 1;65(1):169–76.

3. Fact Sheets by Cancer [Internet]. [cited 2018 Apr 6]. Available from: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx

3. India Human Papillomavirus and Related Diseases, Summary Report 2017

4. National Centre for Disease Informatics and Research, National Cancer Registry Programme, ICMR. Three Year Report of Population Based Registries, 2009–2011.

6. Leading sites of cancer - Hospital based cancer registry 2012- 2014. National Cancer registry program, Indian Council of Medical Research.

7. Dikshit R, Gupta PC, Ramasundarahettige C, Gajalakshmi V, Aleksandrowicz L, Badwe R, et al. Cancer mortality in India: a nationally representative survey. Lancet Lond Engl. 2012 May 12;379(9828):1807–16.

8. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017 Jan;67(1):7–30.

9. Balasubramaniam G, Sushama S, Rasika B, Mahantshetty U. Hospital-based study of endometrial cancer survival in Mumbai, India. Asian Pac J Cancer Prev APJCP. 2013;14(2):977–80.

10. Maheshwari A, Kumar N, Mahantshetty U. Gynecological cancers: A summary of published Indian data. South Asian J Cancer. 2016;5(3):112–20.

11. (3) Current Status of Cancer Burden: Global and Indian Scenario [Internet]. [cited 2018 May 12]. Available from: https://www.researchgate.net/publication/304705330_Current_Status_of_Cancer_Burden_Global_and_Indian_Scenario

12. Dessai SB, Adrash D, Geetha M, Arvind S, Bipin J, Nayanar S, et al. Pattern of care in operable endometrial cancer treated at a rural-based tertiary care cancer center. Indian J Cancer. 2016 Jul 1;53(3):416.

13. Barbosa MS, Schlegel R. The E6 and E7 genes of HPV-18 are sufficient for inducing two-stage in vitro transformation of human keratinocytes. Oncogene. 1989 Dec;4(12):1529–32.

14. Burger RA, Monk BJ, Kurosaki T, Anton-Culver H, Vasilev SA, Berman ML, et al. Human papillomavirus type 18: association with poor prognosis in early stage cervical cancer. J Natl Cancer Inst. 1996 Oct 2;88(19):1361–8.

15. Schwartz SM, Daling JR, Shera KA, Madeleine MM, McKnight B, Galloway DA, et al. Human papillomavirus and prognosis of invasive cervical cancer: a population-based study. J Clin Oncol Off J Am Soc Clin Oncol. 2001 Apr 1;19(7):1906–15.

16. Bayo S, Bosch FX, de Sanjosé S, Muñoz N, Combita AL, Coursaget P, et al. Risk factors of invasive cervical cancer in Mali. Int J Epidemiol. 2002 Feb;31(1):202–9.

17. Louie KS, Sanjose S de, Diaz M, Castellsagué X, Herrero R, Meijer CJ, et al. Early age at first sexual intercourse and early pregnancy are risk factors for cervical cancer in developing countries. Br J Cancer. 2009 Apr;100(7):1191–7.

18. Castle PE. How Does Tobacco Smoke Contribute to Cervical Carcinogenesis? J Virol. 2008 Jun;82(12):6084–6.

19. Fonseca-Moutinho JA. Smoking and Cervical Cancer. ISRN Obstet Gynecol [Internet]. 2011;2011. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3140050/

20. Stone KM, Zaidi A, Rosero-Bixby L, Oberle MW, Reynolds G, Larsen S, et al. Sexual behavior, sexually transmitted diseases, and risk of cervical cancer. Epidemiol Camb Mass. 1995 Jul;6(4):409–14.

21. Ghebre RG, Grover S, Xu MJ, Chuang LT, Simonds H. Cervical cancer control in HIV-infected women: Past, present and future. Gynecol Oncol Rep. 2017 Jul 21;21:101–8.

22. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep. 1992 Dec 18;41(RR-17):1–19.

23. Sorosky JI. Endometrial cancer. Obstet Gynecol. 2008 Feb;111(2 Pt 1):436–47.

24. Alektiar KM, Venkatraman E, Abu-Rustum N, Barakat RR. Is endometrial carcinoma intrinsically more aggressive in elderly patients? Cancer. 2003 Dec 1;98(11):2368–77.

25. Ali AT. Risk factors for endometrial cancer. Ceska Gynekol. 2013 Nov;78(5):448–59.

26. Rice LW. Hormone prevention strategies for breast, endometrial and ovarian cancers. Gynecol Oncol. 2010 Aug 1;118(2):202–7.

27. Reis N, Beji NK. Risk factors for endometrial cancer in Turkish women: results from a hospital-based case-control study. Eur J Oncol Nurs Off J Eur Oncol Nurs Soc. 2009 Apr;13(2):122–7.

28. Parazzini F, La Vecchia C, Moroni S, Chatenoud L, Ricci E. Family history and the risk of endometrial cancer. Int J Cancer. 1994 Nov 15;59(4):460–2.

29. Lucenteforte E, Talamini R, Montella M, Dal Maso L, Pelucchi C, Franceschi S, et al. Family history of cancer and the risk of endometrial cancer. Eur J Cancer Prev Off J Eur Cancer Prev Organ ECP. 2009 Apr;18(2):95–9.

30. Lu KH, Schorge JO, Rodabaugh KJ, Daniels MS, Sun CC, Soliman PT, et al. Prospective determination of prevalence of lynch syndrome in young women with endometrial cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2007 Nov 20;25(33):5158–64.

31. Hampel H, Stephens JA, Pukkala E, Sankila R, Aaltonen LA, Mecklin J-P, et al. Cancer risk in hereditary nonpolyposis colorectal cancer syndrome: later age of onset. Gastroenterology. 2005 Aug;129(2):415–21.

32. Beiner ME, Finch A, Rosen B, Lubinski J, Moller P, Ghadirian P, et al. The risk of endometrial cancer in women with BRCA1 and BRCA2 mutations. A prospective study. Gynecol Oncol. 2007 Jan;104(1):7–10.

33. Thompson D, Easton DF, Breast Cancer Linkage Consortium. Cancer Incidence in BRCA1 mutation carriers. J Natl Cancer Inst. 2002 Sep 18;94(18):1358–65.

34. Breast Cancer Linkage Consortium. Cancer risks in BRCA2 mutation carriers. J Natl Cancer Inst. 1999 Aug 4;91(15):1310–6.

35. Wernli KJ, Ray RM, Gao DL, De Roos AJ, Checkoway H, Thomas DB. Menstrual and reproductive factors in relation to risk of endometrial cancer in Chinese women. Cancer Causes Control CCC. 2006 Sep;17(7):949–55.

36. Navaratnarajah R, Pillay OC, Hardiman P. Polycystic ovary syndrome and endometrial cancer. Semin Reprod Med. 2008 Jan;26(1):62–71.

37. Brinton LA, Westhoff CL, Scoccia B, Lamb EJ, Althuis MD, Mabie JE, et al. Causes of infertility as predictors of subsequent cancer risk. Epidemiol Camb Mass. 2005 Jul;16(4):500–7.

38. Pike MC, Peters RK, Cozen W, Probst-Hensch NM, Felix JC, Wan PC, et al. Estrogen-progestin replacement therapy and endometrial cancer. J Natl Cancer Inst. 1997 Aug 6;89(15):1110–6.

39. Feeley K, Wells M. Hormone replacement therapy and the endometrium. J Clin Pathol. 2001 Jun;54(6):435–40.

40. Razavi P, Pike MC, Horn-Ross PL, Templeman C, Bernstein L, Ursin G. Long-term postmenopausal hormone therapy and endometrial cancer. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2010 Feb;19(2):475.

41. Lindemann K, Vatten LJ, Ellstrøm-Engh M, Eskild A. Body mass, diabetes and smoking, and endometrial cancer risk: a follow-up study. Br J Cancer. 2008 May 6;98(9):1582–5.

42. Trentham-Dietz A, Nichols HB, Hampton JM, Newcomb PA. Weight change and risk of endometrial cancer. Int J Epidemiol. 2006 Feb 1;35(1):151–8.

43. Jahanzeb M. Reducing the risk for breast cancer recurrence after completion of tamoxifen treatment in postmenopausal women. Clin Ther. 2007 Aug;29(8):1535–47.

44. Love CD, Muir BB, Scrimgeour JB, Leonard RC, Dillon P, Dixon JM. Investigation of endometrial abnormalities in asymptomatic women treated with tamoxifen and an evaluation of the role of endometrial screening. J Clin Oncol Off J Am Soc Clin Oncol. 1999 Jul;17(7):2050–4.

45. Friberg E, Mantzoros CS, Wolk A. Diabetes and risk of endometrial cancer: a population-based prospective cohort study. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2007 Feb;16(2):276–80.

46. (3) Diabetes and Endometrial Cancer: An Evaluation of the Modifying Effects of Other Known Risk Factors [Internet]. ResearchGate. [cited 2018 May 12]. Available from: https://www.researchgate.net/publication/5777586_Diabetes_and_Endometrial_Cancer_An_Evaluation_of_the_Modifying_Effects_of_Other_Known_Risk_Factors

47. Smith RA, von Eschenbach AC, Wender R, Levin B, Byers T, Rothenberger D, et al. American Cancer Society guidelines for the early detection of cancer: update of early detection guidelines for prostate, colorectal, and endometrial cancers. Also: update 2001--testing for early lung cancer detection. CA Cancer J Clin. 2001 Feb;51(1):38-75-80.

48. Halperin EC, Perez CA, Wazer DE, Brady LW, editors. Perez and Brady's principles and practice of radiation oncology: [includes access to LWWOoncology.com, LWWOncology. 6. ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2013. 1907 p. (Radiation Oncology).

49. Drescher CW, Hopkins MP, Roberts JA. Comparison of the pattern of metastatic spread of squamous cell cancer and adenocarcinoma of the uterine cervix. Gynecol Oncol. 1989 Jun;33(3):340–3.

50. Benhayoune K, El Fatemi H, Bannani A, Melhouf A, Harmouch T. Adenoid cystic carcinoma of cervix: two cases report and review of the literature. Pan Afr Med J [Internet]. 2015 Jan 29;20. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4450047/

51. Kaur P, Khurana A, Chauhan AK, Singh G, Kataria SP, Singh S. Adenoid Cystic Carcinoma of Cervix: Treatment Strategy. J Clin Diagn Res JCDR. 2013 Nov;7(11):2596–7.

52. WHO Classification of Tumours of Female Reproductive Organs. Fourth Edition - WHO - OMS - [Internet]. [cited 2018 Jun 17]. Available from: http://apps.who.int/bookorders/WHP/detart1.jsp?sesslan=1&codlan=1&codcol=70&codcch=4006

53. Conlon N, Leitao MM, Abu-Rustum NR, Soslow RA. Grading uterine endometrioid carcinoma: a proposal that binary is best. Am J Surg Pathol. 2014 Dec;38(12):1583–7.

54. Landoni F, Maneo A, Colombo A, Placa F, Milani R, Perego P, et al. Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. The Lancet. 1997 Aug 23;350(9077):535–40.

55. Berek JS, Hacker NF, editors. Berek & Hacker's gynecologic oncology. Sixth edition. Philadelphia: Wolters Kluwer; 2015. 960 p.

56. Chan JK, Urban R, Cheung MK, Shin JY, Husain A, Teng NN, et al. Lymphadenectomy in endometrioid uterine cancer staging: how many lymph nodes are enough? A study of 11,443 patients. Cancer. 2007 Jun 15;109(12):2454–60.

57. Lutman CV, Havrilesky LJ, Cragun JM, Secord AA, Calingaert B, Berchuck A, et al. Pelvic lymph node count is an important prognostic variable for FIGO stage I and II endometrial carcinoma with high-risk histology. Gynecol Oncol. 2006 Jul;102(1):92–7.

58. Chan JK, Cheung MK, Huh WK, Osann K, Husain A, Teng NN, et al. Therapeutic role of lymph node resection in endometrioid corpus cancer: a study of 12,333 patients. Cancer. 2006 Oct 15;107(8):1823–30.

59. al NN et. The Futility of Systematic Lymphadenectomy in Early-Stage Low-grade Endometrial Cancer. - PubMed - NCBI [Internet]. [cited 2018 Jun 20]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29887702

60. Rotman M, John M, Boyce J. Prognostic factors in cervical carcinoma: implications in staging and management. Cancer. 1981 Jul;48(2 Suppl):560–7.

61. Chung CK, Nahhas WA, Stryker JA, Curry SL, Abt AB, Mortel R. Analysis of factors contributing to treatment failures in stages IB and IIA carcinoma of the cervix. Am J Obstet Gynecol. 1980 Nov 1;138(5):550–6.

62. Boyce JG, Fruchter RG, Nicastri AD, Deregt RH, Ambiavagar P-C, Reinis M, et al. Vascular invasion in stage I carcinoma of the cervix. Cancer. 1984 Mar 1;53(5):1175–80.

63. Delgado G, Bundy B, Zaino R, Sevin BU, Creasman WT, Major F. Prospective surgical-pathological study of disease-free interval in patients with stage IB squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Gynecol Oncol. 1990 Sep;38(3):352–7.

64. Murakami I, Fujii T, Kameyama K, Iwata T, Saito M, Kubushiro K, et al. Tumor volume and lymphovascular space invasion as a prognostic factor in early invasive adenocarcinoma of the cervix. J Gynecol Oncol. 2012 Jul;23(3):153–8.

65. Rogers L, Siu SSN, Luesley D, Bryant A, Dickinson HO. Adjuvant radiotherapy and chemoradiation after surgery for cervical cancer. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD007583.

66. Rogers L, Siu SSN, Luesley D, Bryant A, Dickinson HO. Radiotherapy and chemoradiation after surgery for early cervical cancer. Cochrane Database Syst Rev. 2012 May 16;5:CD007583.

67. Aalders J, Abeler V, Kolstad P, Onsrud M. Postoperative external irradiation and prognostic parameters in stage I endometrial carcinoma: clinical and histopathologic study of 540 patients. Obstet Gynecol. 1980 Oct;56(4):419–27.

68. Creutzberg CL, Nout RA, Lybeert MLM, Wárlám-Rodenhuis CC, Jobsen JJ, Mens J-WM, et al. Fifteen-year radiotherapy outcomes of the randomized PORTEC-1 trial for endometrial carcinoma. Int J Radiat Oncol Biol Phys. 2011 Nov 15;81(4):e631-638.

69. Keys HM, Roberts JA, Brunetto VL, Zaino RJ, Spirtos NM, Bloss JD, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. Gynecol Oncol. 2004 Mar;92(3):744–51.

70. Nout RA, Smit VTHBM, Putter H, Jürgenliemk-Schulz IM, Jobsen JJ, Lutgens LCHW, et al. Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial. Lancet Lond Engl. 2010 Mar 6;375(9717):816–23.

71. Kong TW, Chang S-J, Paek J, Lee Y, Chun M, Ryu H-S. Risk group criteria for tailoring adjuvant treatment in patients with endometrial cancer: a validation study of the Gynecologic Oncology Group criteria. J Gynecol Oncol. 2015 Jan;26(1):32–9.

72. ASTEC/EN.5 Study Group, Blake P, Swart AM, Orton J, Kitchener H, Whelan T, et al. Adjuvant external beam radiotherapy in the treatment of endometrial cancer (MRC ASTEC and NCIC CTG EN.5 randomised trials): pooled trial results, systematic review, and meta-analysis. Lancet Lond Engl. 2009 Jan 10;373(9658):137–46.

73. de Boer SM, Nout RA, Jürgenliemk-Schulz IM, Jobsen JJ, Lutgens LCHW, van der Steen-Banasik EM, et al. Long-Term Impact of Endometrial Cancer Diagnosis and Treatment on Health-Related Quality of Life and Cancer Survivorship: Results From the Randomized PORTEC-2 Trial. Int J Radiat Oncol Biol Phys. 2015 Nov 15;93(4):797–809.

74. Small W, Beriwal S, Demanes DJ, Dusenbery KE, Eifel P, Erickson B, et al. American Brachytherapy Society consensus guidelines for adjuvant vaginal cuff brachytherapy after hysterectomy. Brachytherapy. 2012 Feb;11(1):58–67.

75. Harkenrider MM, Grover S, Erickson BA, Viswanathan AN, Small C, Kliethermes S, et al. Vaginal brachytherapy for postoperative endometrial cancer: 2014 Survey of the American Brachytherapy Society. Brachytherapy. 2016 Feb;15(1):23–9.

76. Kim H, Kim H, Beriwal S. Is There Any Advantage to 3D Planning for Vaginal Cuff Brachytherapy? Int J Radiat Oncol • Biol • Phys. 2011 Oct 1;81(2):S474.

77. Schoeppel SL, Lavigne ML, Martel MK, McShan DL, Fraass BA, Roberts JA. Three-dimensional treatment planning of intracavitary gynecologic implants: Analysis of ten cases and implications for dose specification. Int J Radiat Oncol • Biol • Phys. 1994 Jan 1;28(1):277–83.

78. Dimopoulos JCA, Petrow P, Tanderup K, Petric P, Berger D, Kirisits C, et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (IV): Basic principles and parameters for MR imaging within the frame of image based adaptive cervix cancer brachytherapy. Radiother Oncol. 2012 Apr;103(1):113–22.

79. Hoskin PJ, Vidler K. Vaginal vault brachytherapy: the effect of varying bladder volumes on normal tissue dosimetry. Br J Radiol. 2000 Aug;73(872):864–6.

80. International Commission on Radiation Units and Measurements (ICRU) [Internet]. [cited 2018 Oct 7]. Available from: https://icru.org/home/reports/dose-and-volume-specification-for-reporting-intracavitary-therapy-in-gynecology-report-38

81. McCloskey SA, Tchabo NE, Malhotra HK, Odunsi K, Rodabaugh K, Singhal P, et al. Adjuvant vaginal brachytherapy alone for high risk localized endometrial cancer as defined by the three major randomized trials of adjuvant pelvic radiation. Gynecol Oncol. 2010 Mar;116(3):404–7.

82. Solhjem MC, Petersen IA, Haddock MG. Vaginal brachytherapy alone is sufficient adjuvant treatment of surgical stage I endometrial cancer. Int J Radiat Oncol Biol Phys. 2005 Aug 1;62(5):1379–84.

83. Holloway CL, Macklin EA, Cormack RA, Viswanathan AN. Should the organs at risk be contoured in vaginal cuff brachytherapy? Brachytherapy. 2011 Aug;10(4):313–7.

84. Shin KH, Kim TH, Cho JK, Kim J-Y, Park SY, Park S-Y, et al. CT-guided intracavitary radiotherapy for cervical cancer: Comparison of conventional point A plan with clinical target volume-based three-dimensional plan using dose-volume parameters. Int J Radiat Oncol Biol Phys. 2006 Jan 1;64(1):197–204.

85. Kim RY, Shen S, Duan J. Image-based three-dimensional treatment planning of intracavitary brachytherapy for cancer of the cervix: dose-volume histograms of the bladder, rectum, sigmoid colon, and small bowel. Brachytherapy. 2007 Sep;6(3):187–94.

86. Onal C, Arslan G, Topkan E, Pehlivan B, Yavuz M, Oymak E, et al. Comparison of conventional and CT-based planning for intracavitary brachytherapy for cervical cancer: target volume coverage and organs at risk doses. J Exp Clin Cancer Res CR. 2009 Jul 1;28(1):95.

87. Ling CC, Schell MC, Working KR, Jentzsch K, Harisiadis L, Carabell S, et al. CT-assisted assessment of bladder and rectum dose in gynecological implants. Int J Radiat Oncol Biol Phys. 1987 Oct;13(10):1577–82.

88. Hung J, Shen S, De Los Santos JF, Kim RY. Image-based 3D treatment planning for vaginal cylinder brachytherapy: dosimetric effects of bladder filling on organs at risk. Int J Radiat Oncol Biol Phys. 2012 Jul 1;83(3):980–5.

89. Stewart AJ, Cormack RA, Lee H, Xiong L, Hansen JL, O'Farrell DA, et al. Prospective clinical trial of bladder filling and three-dimensional dosimetry in high-dose-rate vaginal cuff brachytherapy. Int J Radiat Oncol Biol Phys. 2008 Nov 1;72(3):843–8.

# ANNEXURE

## A. Proposed Protocol for Image Guided Vaginal Brachytherapy (IG-VBT)

i. Complete clinical and gynecological assessment to be done in OPD and total length of vaginal to be measured. A surrogate for the mould applicator is desirable to be used to determine the vaginal length and diameter.

ii. Patient must void completely and then drink 1 litre of water gradually (with 30ml of oral contrast) prior to planning CT.

iii. Planning CT to be done after 1 hour of voiding. CT to be taken in supine position and applicator must be placed in treatment position and fastened with T-bandage to minimize movements.

iv. 2-3mm CT slices is recommended and region of interest must be from L5/S1 to below the ischial tuberosity.

v. Images to be transferred to treatment planning system for contouring.

vi. During target volume delineation, vaginal mucosal treatment length to be determined by delineating upper 2/3$^{rd}$ of the total vaginal mucosal length as assessed prior to planning and correlating with CT based anatomy. Mould surface should be contoured and CTV should be an isometric 5mm expansion from the target delineated.

vii. Organs at risk (bladder, rectum, bowel and sigmoid) to be contoured as per RTOG guidelines for normal pelvic organ contouring.

viii. An appropriate planning system to be used for brachytherapy planning and optimisation. Single or multiple channel applicator to be reconstructed as per the institutional protocol.

ix. Dose optimisation to be done by altering the dwell positions and dwell time by volume-based optimisation. CTV dose coverage is aimed to achieve at least 90% of the prescribed dose to 95% of the target volume (D95 > 90%). D2cc to organs at risk must be kept as low as possible.

x. D90, D95, V100 & V150 to be recorded for CTVsurface & CTV0.5depth.

xi. Dose to 0.1cc, 1cc, 2cc and 5cc of bladder, rectum, sigmoid colon and small bowel to be recorded.

xii. Cumulative EQD2 for target and OARs to be calculated and reported.

xiii. Patient is instructed to follow the same bladder protocol as for planning CT and is to be treated with the optimised plan.

xiv. Repeat CTs and replaning are generally not recommended and the 1$^{st}$ fraction plan may to be used for subsequent fractions.

# B. IRB approval

**OFFICE OF RESEARCH**
**INSTITUTIONAL REVIEW BOARD (IRB)**
**CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

**Dr. B.J. Prashantham,** M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

**Dr. Anna Benjamin Pulimood,** M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

**Dr. Biju George,** M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

April 24, 2017

Dr. Jeyaanth.P.V,
PG registrar,
Department of Radiotherapy,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant New Submission:**
Dosimetric comparison of 3D treatment planning and conventional planning in post-operative vaginal mould brachytherapy (VBT) for patients with gynecological malignancies
Jeyaanth.P.V, PG registrar, Employment Number: 21293, Dr. Thomas Samuel Ram Employment Number: 28155, Professor, Dr. Saikat Das, Associate Professor, Emp. No. : 20423, Dr. Jebakarunya Reddy, Emp. No. : 32230, Assistant Professor, Dr. Arvind.S.Murthy, Emp. No. : 80031, Senior Resident, Mr. Henry Finlay Godson, Emp. No. : 31512, Lecturer, Department of Radiotherapy. MsReka K, Employment No.:32547, Senior Demonstrator, Department of Biostatistics.

Ref: IRB Min. No. 10488 [OBSERV] dated 05.01.2017

Dear Dr. Jeyaanth.P.V,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

**Dr. BIJU GEORGE**
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

CC: Dr. Thomas Samuel Ram, Professor, Radiotherapy, CMC

1 of 5

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

# OFFICE OF RESEARCH
# INSTITUTIONAL REVIEW BOARD (IRB)
# CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

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Ref: IRB Min. No. 10488 [OBSERV] dated 05.01.2017

Dear Dr. Jeyaanth.P.V,

The Institutional Review Board **(Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Dosimetric comparison of 3D treatment planning and conventional planning in post-operative vaginal mould brachytherapy (VBT) for patients with gynecological malignancies" on January 05th 2017.

The Committee reviewed the following documents:

1. IRB Application format
2. Consent forms Information Sheets (Tamil, English, Hindi)
3. Cvs of Drs. Arvind, Jebakarunya, Jeyaanth, Saikat Das, Thomas Ram and Ms. Rekha
4. No. of documents 1- 3.

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on January 05th 2017 in the BRTC Conference Room, Christian Medical College, Bagayam, Vellore 632002.



Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
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**Dr. Biju George,** M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

| Name | Qualification | Designation | Affiliation |
|---|---|---|---|
| Dr. Biju George | MBBS, MD, DM | Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore | Internal, Clinician |
| Dr. B. J. Prashantham | MA(Counseling Psychology), MA (Theology), Dr. Min (Clinical Counselling) | Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore | External, Social Scientist |
| Dr. Ratna Prabha | MBBS, MD (Pharma) | Associate Professor, Clinical Pharmacology, CMC, Vellore | Internal, Pharmacologist |
| Dr. Rekha Pai | BSc, MSc, PhD | Associate Professor, Pathology, CMC, Vellore | Internal, Basic Medical Scientist |
| Rev. Joseph Devaraj | BSc, BD | Chaplaincy Department, CMC, Vellore | Internal, Social Scientist |
| Mr. C. Sampath | BSc, BL | Advocate, Vellore | External, Legal Expert |
| Dr. Simon Pavamani | MBBS, MD | Professor, Radiotherapy, CMC, Vellore | Internal, Clinician |
| Dr. Jayaprakash Muliyil | BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC | Retired Professor, Vellore | External, Scientist &Epidemiologist |
| Ms. Grace Rebekha | M.Sc., (Biostatistics) | Lecturer, Biostatistics, CMC, Vellore | Internal, Statistician |
| Mrs. Pattabiraman | BSc, DSSA | Social Worker, Vellore | External, Lay Person |
| Mrs. Sheela Durai | MSc Nursing | Professor, Medical Surgical Nursing, CMC, Vellore | Internal, Nurse |



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Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

| | | | |
|---|---|---|---|
| Dr. Balamugesh | MBBS, MD(Int Med), DM, FCCP (USA) | Professor, Pulmonary Medicine, CMC, Vellore | Internal, Clinician |
| Dr. Santhanam Sridhar | MBBS, DCH, DNB | Professor, Neonatology, CMC, Vellore | Internal, Clinician |
| Mrs. Emily Daniel | MSc Nursing | Professor, Medical Surgical Nursing, CMC, Vellore | Internal, Nurse |
| Dr. Mathew Joseph | MBBS, MCH | Professor, Neurosurgery, CMC, Vellore | Internal, Clinician |
| Dr. Thomas V Paul | MBBS, MD, DNB, PhD | Professor,Endocrinology, CMC, Vellore | Internal, Clinician |
| Dr. Vivek Mathew | MD (Gen. Med.) DM (Neuro) Dip. NB (Neuro) | Professor, Neurology, CMC, Vellore | Internal, Clinician |
| Dr Sneha Varkki | MBBS, DCH, DNB | Professor, Paediatrics, CMC, Vellore | Internal, Clinician |
| Dr. Sathish Kumar | MBBS, MD, DCH | Professor, Child Health, CMC, Vellore | Internal, Clinician |

approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Dosimetric comparison of 3D treatment planning and conventional planning in post-operative vaginal mould brachytherapy (VBT) for patients with gynecological malignancies."on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).



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Chairperson, Research Committee & Principal

**Dr. Biju George,** M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

*Fluid Grant Allocation:*

*A sum of 1,00,000/- INR (Rupees One Lakh Only) will be granted for 2 years. 50,000/- INR (Rupees Fifty Thousand only) will be granted for 12 months as an 1st Installment. The rest of the 50,000/- INR (Rupees Fifty Thousand only) each will be released at the end of the first year as 2 nd Installment.*

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee), Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.



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C. Consent form

**Informed Consent Form**

Informed Consent form to participate in a research study

**Study Title: Dosimetric comparison of 3D treatment planning and conventional planning in post-operative vaginal mould brachytherapy for patients with gynecological malignancies**

**Study Number:** _____

**Subject's Name/Hosp ID:** _____ **Age:** _____

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Investigator's signature: _____

Witness: _____

Date: _____/_____/_____

Date: _____/_____/_____

# D. Information sheet

Christian Medical College, Vellore

Department of Radiotherapy

**Dosimetric comparison of 3D treatment planning and conventional planning in post-operative vaginal mould brachytherapy for patients with gynecological malignancies**

You are being requested to participate in a study which will assess the radiation dose delivered to tumour tissue and normal organs by 3D CT based planning while you undergo vaginal mould brachytherapy.

You will be undergoing treatment of your condition as per current standard practice. Brachytherapy assessment will be done as out-patient basis and you will be asked to come for treatment with a few preparatory instructions. You will undergo vaginal mould application and a CT scan will be taken. Following which, tumour volumes and normal organs are contoured on the CT scan and the dose optimisation is done by medical physicist with a goal of delivering maximum dose to the tumour and minimal possible dose to the adjacent normal tissues.

**Can you withdraw from this study after it starts?**

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your treatment at this hospital in any way.

**What will happen if you develop any study related injury?**

We do not expect any injury to occur.

**Will you have to pay for the test?**

You have to pay the vaginal mould brachytherapy treatment as it is considered the standard of care. As we are investigating the role of CT based planning, you don't have to pay for CT scan.

**Will my treatment details be kept confidential?**

All your treatment details will not be revealed to any third party. The results will be reviewed only by people associated with the study.

**Will your personal details be kept confidential?**

The results of this study will be published in a medical journal but you will not be identified by

name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

## E. Data collection sheet

### Data Sheet

**Study Title: Dosimetric comparison of 3D treatment planning and conventional planning in post-operative vaginal mould brachytherapy for patients with gynecological malignancies**

**Study Number:**

**Hospital Number:_____ Age: _____**

**Diagnosis & stage:**

**Dose & fractions planned:**

**EBRT – Y / N If yes – dose & fraction -**

**Technique -**

2D based plan

| Fraction # | Bladder status | Rectum status | CTV surface | | | | | CTV0.5 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Volume | D90 | D95 | V100 | V150 | Volume | D90 | D95 | V100 | V150 |
| | | | | | | | | | | | | |
| | | | | | | | | | | | | |
| | | | | | | | | | | | | |

| Fraction # | Bladder | | | | | Rectum | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Volume | D0.1 | D1 | D2 | D5 | Volume | D0.1 | D1 | D2 | D5 |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| Fraction # | Sigmoid | | | | | SI | | | | |
| | Volume | D0.1 | D1 | D2 | D5 | Volume | D0.1 | D1 | D2 | D5 |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |

3D based plan

| Fraction # | Bladder status | Rectum status | CTV surface | | | | | CTV0.5 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Volume | D90 | D95 | V100 | V150 | Volume | D90 | D95 | V100 | V150 |
| | | | | | | | | | | | | |
| | | | | | | | | | | | | |
| | | | | | | | | | | | | |

| Fraction # | Bladder | | | | | Rectum | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Volume** | D0.1 | D1 | D2 | D5 | **Volume** | D0.1 | D1 | D2 | D5 |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| **Fraction #** | **Sigmoid** | | | | | **SI** | | | | |
| | **Volume** | D0.1 | D1 | D2 | D5 | **Volume** | D0.1 | D1 | D2 | D5 |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |

Toxicity profile (CTCAE v4.0)

| Timeline | GI toxicity | | GU toxicity | | Comments |
|---|---|---|---|---|---|
| | Adverse event | Grade | Adverse event | Grade | |
| 6 weeks post RT | | | | | |
| 12 weeks post RT | | | | | |

# F. Excel Sheet of Data

| H. No | Study Number | Age | b.Diagnosis (1 – Carcinoma endometrium, 2 -Carcinoma cervix, 3 – Carcinoma cervical stump) | EBRT (1 - Yes, 2 - No) | Technique (1- IMRT/VMAT, 2 - 3DCRT, 3 - 2D, 4 - NA) |
|---|---|---|---|---|---|
| | | | | Nominal | Nominal |
| | | | | | |
| 710145G | VBT1 | 40 | 1 | 1 | 1 |
| 710145G | VBT2 | 40 | 1 | 1 | 1 |
| 710145G | VBT3 | 40 | 1 | 1 | 1 |
| 746435G | VBT4 | 68 | 2 | 2 | 4 |
| 746435G | VBT5 | 68 | 2 | 2 | 4 |
| 655586G | VBT6 | 36 | 1 | 1 | 1 |
| 698961G | VBT7 | 63 | 3 | 1 | 1 |
| 764902G | VBT8 | 46 | 3 | 1 | 1 |
| 540465G | VBT9 | 53 | 3 | 1 | 1 |
| 751560G | VBT10 | 40 | 2 | 1 | 1 |
| 751560G | VBT11 | 40 | 2 | 1 | 1 |
| 776949G | VBT13 | 41 | 3 | 1 | 3 |
| 776949G | VBT14 | 41 | 3 | 1 | 3 |
| 707016G | VBT15 | 49 | 1 | 1 | 1 |
| 790084G | VBT16 | 43 | 2 | 1 | 1 |
| 688238G | VBT17 | 49 | 1 | 1 | 1 |
| 688238G | VBT18 | 49 | 1 | 1 | 1 |
| 688238G | VBT19 | 49 | 1 | 1 | 1 |
| 753043G | VBT20 | 54 | 1 | 1 | 1 |
| 753043G | VBT21 | 54 | 1 | 1 | 1 |
| 007086D | VBT22 | 41 | 1 | 2 | 4 |
| 007086D | VBT23 | 41 | 1 | 2 | 4 |
| 789150G | VBT24 | 67 | 1 | 1 | 1 |
| 789150G | VBT25 | 67 | 1 | 1 | 1 |
| 820293G | VBT26 | 50 | 3 | 1 | 1 |
| 820293G | VBT27 | 50 | 3 | 1 | 1 |
| 820293G | VBT28 | 50 | 3 | 1 | 1 |
| 759861G | VBT29 | 59 | 3 | 1 | 3 |
| 759861G | VBT30 | 59 | 3 | 1 | 3 |
| 759861G | VBT31 | 59 | 3 | 1 | 3 |
| 857690G | VBT32 | 58 | 1 | 2 | 4 |
| 857690G | VBT33 | 58 | 1 | 2 | 4 |
| 857690G | VBT34 | 58 | 1 | 2 | 4 |
| 825820G | VBT35 | 59 | 2 | 1 | 1 |
| 825820G | VBT36 | 59 | 2 | 1 | 1 |
| 845194G | VBT37 | 60 | 1 | 1 | 1 |
| 845194G | VBT38 | 60 | 1 | 1 | 1 |
| 758603G | VBT39 | 66 | 1 | 1 | 1 |
| 758603G | VBT40 | 66 | 1 | 1 | 1 |
| 832087G | VBT41 | 54 | 1 | 1 | 1 |
| 832087G | VBT42 | 54 | 1 | 1 | 1 |
| 832087G | VBT43 | 54 | 1 | 1 | 1 |
| 803531G | VBT44 | 43 | 1 | 1 | 1 |

| | | | | | |
|---|---|---|---|---|---|
| 803531G | VBT45 | 43 | 1 | 1 | 1 |
| 784542G | VBT46 | 46 | 1 | 1 | 2 |
| 784542G | VBT47 | 46 | 1 | 1 | 2 |
| 893572G | VBT48 | 60 | 1 | 2 | 4 |
| 893572G | VBT49 | 60 | 1 | 2 | 4 |
| 893572G | VBT50 | 60 | 1 | 2 | 4 |
| 905099G | VBT51 | 62 | 2 | 1 | 1 |
| 905099G | VBT52 | 62 | 2 | 1 | 1 |
| 566298G | VBT53 | 49 | 2 | 1 | 3 |
| 566298G | VBT54 | 49 | 2 | 1 | 3 |
| 536777G | VBT55 | 34 | 1 | 1 | 2 |
| 536777G | VBT56 | 34 | 1 | 1 | 2 |
| 536777G | VBT57 | 34 | 1 | 1 | 2 |
| 913000G | VBT58 | 44 | 2 | 1 | 2 |
| 913000G | VBT59 | 44 | 2 | 1 | 2 |
| 913000G | VBT60 | 44 | 2 | 1 | 2 |
| 074596D | VBT61 | 40 | 1 | 1 | 1 |
| 074596D | VBT62 | 40 | 1 | 1 | 1 |
| 965091G | VBT63 | 47 | 1 | 2 | 4 |
| 965091G | VBT64 | 47 | 1 | 2 | 4 |
| 893565G | VBT65 | 24 | 1 | 1 | 2 |
| 893565G | VBT66 | 24 | 1 | 1 | 2 |
| 893565G | VBT67 | 24 | 1 | 1 | 2 |
| 850348G | VBT68 | 67 | 1 | 1 | 2 |
| 850348G | VBT69 | 67 | 1 | 1 | 2 |
| 958893G | VBT70 | 55 | 1 | 1 | 1 |
| 958893G | VBT71 | 55 | 1 | 1 | 1 |
| 975633G | VBT72 | 45 | 2 | 1 | 2 |
| 975633G | VBT73 | 45 | 2 | 1 | 2 |
| 975633G | VBT74 | 45 | 2 | 1 | 2 |
| 919773G | VBT75 | 49 | 2 | 1 | 3 |
| 919773G | VBT76 | 49 | 2 | 1 | 3 |
| 204923B | VBT77 | 45 | 2 | 1 | 3 |
| 204923B | VBT78 | 45 | 2 | 1 | 3 |
| 247232B | VBT79 | 60 | 1 | 2 | 4 |
| 247232B | VBT80 | 60 | 1 | 2 | 4 |
| 247232B | VBT81 | 60 | 1 | 2 | 4 |
| 730537C | VBT82 | 63 | 1 | 1 | 1 |
| 730537C | VBT83 | 63 | 1 | 1 | 1 |
| 915425G | VBT84 | 42 | 2 | 1 | 1 |
| 915425G | VBT85 | 42 | 2 | 1 | 1 |
| 387150F | VBT86 | 69 | 2 | 1 | 1 |
| 387150F | VBT87 | 69 | 2 | 1 | 1 |
| 004184H | VBT88 | 46 | 3 | 1 | 1 |
| 004184H | VBT89 | 46 | 3 | 1 | 1 |
| 008467H | VBT90 | 48 | 2 | 1 | 1 |
| 008467H | VBT91 | 48 | 2 | 1 | 1 |
| 721228C | VBT92 | 55 | 1 | 1 | 3 |
| 721228C | VBT93 | 55 | 1 | 1 | 3 |

| | | | | |
|---|---|---|---|---|
| 2 | 2 | 1 | 2 | 1 |
| 1 | 2 | 2 | 1 | 2 |
| 1 | 2 | 2 | 2 | 1 |
| 3 | 1 | 2 | 1 | 2 |
| 3 | 1 | 2 | 2 | 1 |
| 3 | 1 | 2 | 3 | 1 |
| 1 | 2 | 2 | 1 | 2 |
| 1 | 2 | 2 | 2 | 1 |
| 1 | 3 | 2 | 1 | 2 |
| 1 | 3 | 2 | 2 | 1 |
| 2 | 1 | 1 | 1 | 2 |
| 2 | 1 | 1 | 2 | 1 |
| 2 | 1 | 1 | 3 | 1 |
| 1 | 3 | 2 | 1 | 2 |
| 1 | 3 | 2 | 2 | 1 |
| 1 | 3 | 2 | 3 | 1 |
| 1 | 3 | 2 | 1 | 2 |
| 1 | 3 | 2 | 2 | 1 |
| 3 | 3 | 1 | 1 | 2 |
| 3 | 3 | 1 | 2 | 2 |
| 2 | 2 | 1 | 1 | 2 |
| 2 | 2 | 1 | 2 | 1 |
| 2 | 2 | 1 | 3 | 2 |
| 1 | 3 | 1 | 1 | 1 |
| 1 | 3 | 1 | 2 | 2 |
| 1 | 1 | 2 | 1 | 2 |
| 1 | 1 | 2 | 2 | 1 |
| 1 | 1 | 2 | 1 | 2 |
| 1 | 1 | 2 | 2 | 1 |
| 1 | 1 | 2 | 3 | 1 |
| 1 | 1 | 2 | 1 | 2 |
| 1 | 1 | 2 | 2 | 1 |
| 1 | 3 | 2 | 1 | 2 |
| 1 | 3 | 2 | 2 | 1 |
| 3 | 3 | 1 | 1 | 2 |
| 3 | 3 | 1 | 2 | 1 |
| 3 | 3 | 1 | 1 | 2 |
| 1 | 2 | 2 | 1 | 2 |
| 1 | 2 | 2 | 2 | 1 |
| 1 | 2 | 2 | 1 | 2 |
| 1 | 2 | 2 | 2 | 1 |
| 1 | 1 | 2 | 1 | 2 |
| 1 | 1 | 2 | 2 | 1 |
| 1 | 1 | 2 | 1 | 2 |
| 1 | 1 | 2 | 2 | 1 |
| 1 | 1 | 2 | 1 | 2 |
| 1 | 1 | 2 | 2 | 1 |
| 1 | 1 | 2 | 1 | 2 |
| 1 | 1 | 2 | 2 | 1 |

| Bladder Volume | Rectum Volume | Sigmoid Volume | Bowel Volume | 2D | 2D_CTVsurface D90 |
|---|---|---|---|---|---|
| Continous | Continous | Continous | Continous | | Continous |
| | | | | | |
| 318 | 55 | 39.4 | 257.1 | | 178.4 |
| 55.2 | 20.6 | 36.1 | 383 | | 202 |
| 140.1 | 74.7 | 13.5 | 231.5 | | 175.45 |
| 369.4 | 86.7 | 12.2 | 331.7 | | 148.97 |
| 268.8 | 41.7 | 37.2 | 293.7 | | 148.83 |
| 644 | 27.3 | 38.7 | 383.4 | | 173.5 |
| 244.3 | 32.4 | 56.7 | 372.4 | | 163.31 |
| 378.8 | 22.5 | 11.9 | 176.3 | | 194.28 |
| 169.9 | 51.8 | 18.4 | 488 | | 154.47 |
| 148.2 | 69.9 | 27.7 | 481 | | 194.32 |
| 23 | 37.4 | 61.2 | 557 | | 157.06 |
| 231.7 | 33.8 | 13.1 | 294 | | 146.39 |
| 45.1 | 36.3 | 21.2 | 334 | | 155 |
| 633 | 81.1 | 21.5 | 433 | | 138 |
| 331.9 | 51 | 47.4 | 219 | | 194.28 |
| 177.1 | 53.5 | 54.4 | 377.5 | | 153.01 |
| 36.2 | 22.5 | 88.1 | 354.7 | | 163.01 |
| 138.6 | 51.3 | 41.6 | 245.4 | | 160.81 |
| 44.9 | 54.9 | 40.3 | 570 | | 165.7 |
| 34.1 | 48.2 | 39.2 | 637.4 | | 159.31 |
| 142.2 | 34.5 | 17.3 | 443 | | 161.68 |
| 38.3 | 17 | 15.7 | 516 | | 151.21 |
| 624.8 | 45.1 | 15.8 | 232 | | 162.49 |
| 203 | 35.8 | 15 | 437 | | 159.86 |
| 137.3 | 27.8 | 28.4 | 267 | | 158.13 |
| 44.9 | 26.3 | 27.7 | 425 | | 145.37 |
| 92.3 | 23.7 | 36 | 363 | | 145.57 |
| 389.2 | 65.1 | 20.6 | 340 | | 156.94 |
| 134.2 | 64.3 | 13.5 | 494.3 | | 161.09 |
| 190.4 | 89.1 | 11.7 | 514.3 | | 150.72 |
| 441.7 | 29.6 | 16.2 | 433 | | 171.7 |
| 81.4 | 27.7 | 11.8 | 626 | | 150.99 |
| 51.3 | 27.6 | 14.1 | 647 | | 168.55 |
| 180.4 | 62.9 | 29.5 | 371 | | 154.24 |
| 38.9 | 53.8 | 44.7 | 482 | | 156.17 |
| 327.6 | 28.7 | 18.8 | 405 | | 159.57 |
| 63.9 | 23.7 | 22 | 678 | | 157.19 |
| 153.7 | 47.7 | 25.9 | 537 | | 146.89 |
| 45.8 | 23.6 | 34.1 | 675.5 | | 140.61 |
| 659.7 | 67.7 | 35.7 | 217 | | 160.28 |
| 48.7 | 73.2 | 21.6 | 489 | | 162.73 |
| 246.6 | 50.7 | 25.6 | 312 | | 152.64 |
| 334.5 | 30.5 | 23.5 | 321.3 | | 160.89 |

| | | | | | |
|---|---|---|---|---|---|
| 39.1 | 36.5 | 33.2 | 489.7 | | 162.77 |
| 629.6 | 39.1 | 23.7 | 374 | | 156.31 |
| 70.5 | 37 | 22.3 | 560.7 | | 146.12 |
| 284.4 | 60 | 67.8 | 485 | | 151.48 |
| 35.2 | 69.3 | 64.2 | 737.5 | | 144.31 |
| 34.4 | 65.3 | 57.9 | 757.4 | | 144.87 |
| 371.4 | 75.8 | 26.7 | 499.7 | | 153.14 |
| 135.7 | 79.3 | 26.9 | 626.8 | | 137.73 |
| 249.4 | 63 | 49.7 | 496.6 | | 148.32 |
| 93.4 | 50.4 | 40.1 | 748 | | 142.76 |
| 402.7 | 55.8 | 44.7 | 227.6 | | 149.37 |
| 73.3 | 45.9 | 54.4 | 489 | | 154.34 |
| 31.1 | 39.6 | 56.7 | 518.6 | | 153.59 |
| 553.7 | 33.4 | 47.5 | 590.7 | | 153.76 |
| 51.4 | 56.3 | 49.6 | 757.8 | | 154.35 |
| 61.3 | 58.9 | 65.1 | 739 | | 156.66 |
| 618.7 | 68 | 33.6 | 125.6 | | 142.39 |
| 67.1 | 72.8 | 35.9 | 424.8 | | 153.76 |
| 318 | 44.5 | 125 | 487.9 | | 161.89 |
| 187.1 | 55.6 | 115.6 | 781.2 | | 168 |
| 550 | 33.6 | 18.1 | 85.2 | | 165.8 |
| 39 | 30.4 | 20.3 | 394.7 | | 161.76 |
| 210 | 28.4 | 23.6 | 165.8 | | 161.67 |
| 138.9 | 30.3 | 20.8 | 429.8 | | 165.22 |
| 59.3 | 34.4 | 19.8 | 464.8 | | 163.53 |
| 309.3 | 46.1 | 26.2 | 292.2 | | 169.03 |
| 24.4 | 32.7 | 23.2 | 405 | | 144.96 |
| 423.9 | 49.7 | 35.1 | 564.7 | | 163.58 |
| 60.7 | 55.5 | 51.8 | 719.7 | | 165.42 |
| 104.2 | 62 | 34.9 | 615 | | 156.36 |
| 552.8 | 38.2 | 47.2 | 598 | | 148.82 |
| 120.9 | 48.2 | 44.2 | 641.7 | | 151.7 |
| 266.6 | 67.6 | 37.8 | 468 | | 152.55 |
| 74.8 | 57.6 | 45 | 818 | | 152.61 |
| 568.1 | 42.1 | 28.1 | 429 | | 160.16 |
| 55.6 | 37.5 | 30.3 | 565 | | 155.5 |
| 365.8 | 42.5 | 25.3 | 469 | | 163 |
| 405.4 | 56.5 | 27 | 560 | | 148.46 |
| 89.5 | 51 | 49.1 | 787 | | 148.62 |
| 669.5 | 32 | 19.7 | 255 | | 160.19 |
| 99.5 | 24.9 | 31.2 | 465 | | 152.92 |
| 230.5 | 62.9 | 29.5 | 371 | | 142.39 |
| 60.6 | 53.8 | 44.7 | 482 | | 153.76 |
| 416.4 | 42.8 | 25.8 | 511.2 | | 156.38 |
| 41.2 | 27.6 | 28.6 | 854.9 | | 148.13 |
| 181.9 | 25.6 | 26.4 | 336 | | 158.86 |
| 42.2 | 20.6 | 36.4 | 404.6 | | 159.74 |
| 297.7 | 36.1 | 26.2 | 282 | | 168.03 |
| 54.4 | 42.3 | 24.2 | 367.7 | | 143.96 |

| 2D_CTVsurface_D95 | 2D_CTVsurface_V100 | 2D_CTVsurface_V150 | 2D_CTV0.5_D90 | 2D_CTV0.5_D95 | 2D_CTV0.5_V100 | 2D_CTV0.5_V150 |
|---|---|---|---|---|---|---|
| Continous | Continous | Continous | Continous | Continous | Continous | Continous |
| | | | | | | |
| 164 | 100 | 98 | 115.1 | 107.36 | 97.8 | 65.86 |
| 190.3 | 100 | 99.8 | 124.51 | 117.36 | 99.71 | 70.83 |
| 163.22 | 100 | 98.2 | 124.57 | 117.36 | 99.71 | 70.83 |
| 137.89 | 99.96 | 89.47 | 100.05 | 93.97 | 90.43 | 52.36 |
| 135.9 | 99.95 | 89.44 | 99.04 | 91.82 | 89.13 | 50.1 |
| 160.68 | 100 | 98.25 | 110.01 | 102.73 | 96.45 | 59.41 |
| 151.64 | 99.94 | 95.55 | 103.45 | 96.42 | 92.65 | 53.97 |
| 179.13 | 100 | 99.21 | 121.9 | 113.9 | 98.7 | 69.72 |
| 139.89 | 99.96 | 96.59 | 106 | 100.7 | 96 | 55.45 |
| 182.2 | 100 | 99.67 | 116.42 | 108.74 | 98.2 | 64.56 |
| 148.91 | 100 | 94.44 | 105.27 | 99.07 | 94.35 | 55.26 |
| 135.14 | 99.98 | 88.08 | 95.35 | 88.26 | 85.73 | 48.72 |
| 138 | 99 | 91.8 | 98.6 | 90.4 | 88 | 52.3 |
| 126 | 88.46 | 83.62 | 92.11 | 85.19 | 82.39 | 45.99 |
| 179.13 | 100 | 99.21 | 121.9 | 113.9 | 98.7 | 69.72 |
| 132.11 | 99.58 | 90.93 | 101.48 | 93.02 | 91.06 | 54.1 |
| 141.13 | 99.73 | 93.47 | 101.36 | 92.86 | 90.98 | 53.68 |
| 146.92 | 99.9 | 94.21 | 102.86 | 96.7 | 92.57 | 53.98 |
| 155 | 100.04 | 96.79 | 102.62 | 96.29 | 92.24 | 53.12 |
| 145.57 | 99.85 | 93.74 | 101.18 | 94.51 | 91 | 54.05 |
| 146.79 | 100.03 | 94.2 | 104.21 | 97.37 | 93.32 | 55.69 |
| 134.55 | 99.73 | 90.53 | 101.04 | 94.04 | 90.92 | 53.31 |
| 136.4 | 99.75 | 92.64 | 100.79 | 90.68 | 90.92 | 52.1 |
| 141.77 | 99.96 | 92.97 | 100.75 | 92.48 | 90.5 | 54.76 |
| 145.77 | 99.86 | 93.56 | 103.26 | 96.24 | 92.47 | 55.11 |
| 128.69 | 99.78 | 87.59 | 96.4 | 88.96 | 96.23 | 48.17 |
| 126.97 | 99.53 | 87.96 | 97.57 | 88.58 | 87.76 | 50.17 |
| 140.22 | 99.9 | 92.69 | 96.9 | 89.22 | 87.39 | 49.57 |
| 148.29 | 100 | 94.4 | 97.35 | 90.41 | 87.04 | 49.72 |
| 137.27 | 99.65 | 90.39 | 93.32 | 86.79 | 82.8 | 46.43 |
| 156.52 | 99.87 | 72.72 | 102.4 | 94.64 | 91.85 | 53.98 |
| 125.42 | 98.69 | 90.2 | 99.76 | 86.05 | 89.88 | 54.97 |
| 144.78 | 99.84 | 92.18 | 102.69 | 93.77 | 91.34 | 53.99 |
| 141.45 | 100.05 | 92.09 | 100.1 | 93.46 | 90.09 | 52.08 |
| 140.56 | 100.02 | 92.29 | 101.14 | 93.53 | 90.97 | 51.99 |
| 147.76 | 100.04 | 94.24 | 96.14 | 88.77 | 86.6 | 48.07 |
| 144.39 | 99.94 | 93.06 | 92.7 | 85.89 | 83.19 | 46.35 |
| 129.56 | 99.55 | 88.67 | 97.21 | 88.58 | 87.77 | 50.92 |
| 124.28 | 99.57 | 84.43 | 92.09 | 84.3 | 82.12 | 46.85 |
| 149.72 | 99.8 | 94.9 | 103.79 | 97 | 93.05 | 52.4 |
| 153.78 | 100 | 96.7 | 101.88 | 94.69 | 91.37 | 52.93 |
| 141.95 | 100 | 91.32 | 102.74 | 97.08 | 92.59 | 52.61 |
| 148.05 | 99.82 | 94.38 | 97.7 | 90.49 | 88.03 | 49.89 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 148.36 | 99.99 | 94.56 | 99.25 | 92.02 | 89.88 | 50.84 |
| 138.71 | 99.78 | 92.32 | 100.23 | 92.51 | 90.18 | 52.95 |
| 128.61 | 99.43 | 88.21 | 96.8 | 87.76 | 87.16 | 50.15 |
| 133.04 | 99.44 | 90.57 | 94.17 | 85.42 | 85.07 | 49.85 |
| 125.21 | 99.5 | 87.55 | 91.99 | 82.77 | 82.73 | 47.89 |
| 132.56 | 99.87 | 86.77 | 91.4 | 84.7 | 80.66 | 44.33 |
| 140.08 | 99.97 | 91.68 | 98.62 | 92.41 | 88.61 | 49.94 |
| 126.19 | 99.72 | 82.09 | 89.05 | 83.38 | 77.87 | 43.33 |
| 139.19 | 100.03 | 88.88 | 94.99 | 89.17 | 84.82 | 47.29 |
| 127.83 | 99.89 | 85.6 | 94.37 | 87.5 | 84.21 | 47.12 |
| 147.62 | 100.04 | 94.17 | 96.42 | 89.64 | 86.63 | 49.3 |
| 146.79 | 100.02 | 94.32 | 98.96 | 91.9 | 89.17 | 50.24 |
| 145.53 | 99.99 | 94.13 | 99.48 | 92.28 | 89.52 | 50.27 |
| 140.82 | 99.99 | 91.76 | 99.36 | 92.53 | 89.47 | 51.53 |
| 142.71 | 100.01 | 92.07 | 100.76 | 94.33 | 90.66 | 52.56 |
| 144.26 | 100.04 | 92.95 | 101.14 | 94.41 | 90.94 | 52.19 |
| 129.79 | 98.68 | 86.37 | 93.53 | 86.49 | 84.17 | 47.89 |
| 141.33 | 99.79 | 91.93 | 97.4 | 90.72 | 87.42 | 49.4 |
| 147.96 | 99.97 | 96.76 | 101.88 | 93.66 | 91.35 | 53.3 |
| 154.37 | 100.04 | 95.95 | 98.18 | 91.6 | 88.19 | 49.04 |
| 149.72 | 100 | 94.94 | 101.54 | 94.61 | 91.33 | 52.17 |
| 148.45 | 100.2 | 94.48 | 102.6 | 95.68 | 92.12 | 52.45 |
| 155.6 | 100.05 | 96.1 | 100.98 | 93.35 | 90.74 | 54.42 |
| 152.88 | 100.01 | 95.83 | 97.15 | 91.13 | 87.12 | 48.19 |
| 159.79 | 100.03 | 97.05 | 99.48 | 92.22 | 89.56 | 51.03 |
| 156.52 | 100.04 | 96.62 | 101.99 | 94.44 | 91.6 | 54.13 |
| 127.75 | 99.28 | 88 | 99.46 | 91.06 | 89.57 | 52.19 |
| 149.64 | 100 | 94.88 | 100.77 | 94.89 | 90.72 | 53.52 |
| 142.6 | 99.77 | 93.77 | 102.25 | 93.8 | 91.64 | 54.44 |
| 142.14 | 100 | 92.47 | 100.79 | 93.23 | 90.63 | 53.46 |
| 130.33 | 99.67 | 89.57 | 94.36 | 84.96 | 85.01 | 49.51 |
| 136.09 | 100.02 | 90.09 | 96.93 | 88.48 | 87.38 | 49.89 |
| 143.68 | 100.04 | 93.75 | 99.31 | 91.22 | 89.93 | 50.36 |
| 135.76 | 100 | 91.13 | 96.22 | 88.39 | 86.43 | 49.13 |
| 146.69 | 99.8 | 94.48 | 95.47 | 89.73 | 85.33 | 46.98 |
| 139.9 | 100.5 | 92.62 | 95.14 | 87.22 | 85.63 | 48.44 |
| 150.31 | 99.8 | 95.03 | 100.2 | 90.32 | 90.15 | 55.15 |
| 136.34 | 99.56 | 89.2 | 93.23 | 86.43 | 83.5 | 47.55 |
| 134.87 | 99.66 | 89.35 | 91.1 | 84.11 | 80.86 | 45.79 |
| 146.77 | 99.96 | 93.97 | 100.35 | 93.82 | 90.31 | 52.87 |
| 141.15 | 100.04 | 91.5 | 96.85 | 90.12 | 86.81 | 49.16 |
| 129.79 | 98.68 | 86.37 | 93.53 | 86.49 | 84.17 | 47.89 |
| 141.33 | 99.79 | 91.93 | 97.4 | 90.72 | 87.42 | 49.4 |
| 134.2 | 99.64 | 91.85 | 99.1 | 91.05 | 93.21 | 58.79 |
| 136.71 | 100 | 88.84 | 99.1 | 91.05 | 93.21 | 58.79 |
| 144.96 | 100 | 93.74 | 99.63 | 92.74 | 89.7 | 52.57 |
| 145.28 | 99.95 | 93.65 | 101.56 | 94.24 | 91.2 | 53.44 |
| 155.52 | 100.04 | 95.62 | 100.99 | 93.44 | 90.5 | 53.13 |
| 128.75 | 99.18 | 87 | 98.46 | 90.06 | 89.57 | 51.19 |

| 2D_Bladder_0.1cc | 2D_Bladder_1cc | 2D_Bladder_2cc | 2D_Bladder_5cc | 2D_Rectum_0.1cc | 2D_Rectum_1cc | 2D_Rectum_2cc |
|---|---|---|---|---|---|---|
| Continous | Continous | Continous | Continous | Continous | Continous | Continous |
| | | | | | | |
| 170.1 | 112.73 | 98.69 | 85.63 | 162.05 | 117.47 | 104.13 |
| 99.5 | 88.97 | 88.33 | 72.68 | 127.13 | 105.04 | 94.89 |
| 179.8 | 121.03 | 110.19 | 93.32 | 136.01 | 115.19 | 106.12 |
| 134.35 | 108.82 | 100.35 | 86.32 | 102.89 | 86.31 | 76.21 |
| 131.56 | 98.18 | 90.49 | 78.89 | 105.27 | 84.89 | 74.61 |
| 161.1 | 133.04 | 122.09 | 106.78 | 112.96 | 96.27 | 87.24 |
| 100.92 | 90.83 | 85.83 | 76.36 | 114.32 | 95.32 | 87.46 |
| 117.47 | 104.7 | 99.01 | 87.39 | 106.9 | 87.88 | 79.87 |
| 49.87 | 35.78 | 31.94 | 26.55 | 109.2 | 99.6 | 90.08 |
| 179.73 | 113.87 | 99.71 | 81.7 | 125.21 | 107.73 | 99.34 |
| 97.55 | 82.72 | 74.48 | 58.93 | 109.89 | 96.5 | 89.22 |
| 123.25 | 108.69 | 102.4 | 89.58 | 106.71 | 86.72 | 77.73 |
| 92.5 | 82.91 | 78.25 | 68.76 | 115.37 | 86.99 | 75.97 |
| 161.19 | 108.36 | 94.37 | 78.38 | 150.39 | 106.56 | 96.68 |
| 117.47 | 104.7 | 99.01 | 87.39 | 106.9 | 87.88 | 79.87 |
| 116.94 | 103.9 | 95.72 | 80.31 | 110.99 | 87.06 | 74.84 |
| 141.35 | 103.66 | 87.75 | 66.38 | 122.45 | 91.16 | 80.05 |
| 135.16 | 104.77 | 94.3 | 79.12 | 113.66 | 98.85 | 88.46 |
| 73.15 | 61.83 | 56.26 | 47.14 | 101.69 | 83.15 | 75.15 |
| 90.11 | 73.77 | 65.6 | 52.28 | 128.88 | 102.58 | 92.42 |
| 117.43 | 94.27 | 85.38 | 69.25 | 117.05 | 93.02 | 80.55 |
| 110.66 | 86.43 | 75.89 | 58.66 | 109.09 | 86.89 | 75.23 |
| 119.07 | 100.26 | 92.16 | 79.8 | 102.01 | 73.85 | 62.86 |
| 135.64 | 110.48 | 99.57 | 82.31 | 99.6 | 78.89 | 68.29 |
| 106.18 | 92.88 | 85.89 | 74.41 | 127.89 | 96.8 | 84.54 |
| 102.73 | 84.29 | 75.77 | 61.39 | 97.74 | 74.17 | 62.07 |
| 92.62 | 68.19 | 60.94 | 49.92 | 93.9 | 73.18 | 61.49 |
| 33.95 | 27.71 | 25.08 | 21.09 | 77.18 | 56.98 | 49.8 |
| 61.76 | 45.28 | 39.15 | 29.96 | 68.3 | 54.57 | 47.28 |
| 30.98 | 26.38 | 24.21 | 20.8 | 55.39 | 45.62 | 41.31 |
| 113.29 | 96.72 | 89.8 | 77.67 | 144.37 | 115.33 | 99.69 |
| 119.3 | 94.93 | 82.98 | 64.49 | 155.96 | 117.58 | 100.7 |
| 93.61 | 72.82 | 63.65 | 49.85 | 121.9 | 96.24 | 83.31 |
| 121.94 | 98.1 | 89.64 | 76.86 | 153.51 | 115.5 | 100.54 |
| 102.2 | 78.37 | 86.22 | 65.9 | 142.52 | 110.16 | 99.05 |
| 88.34 | 73.13 | 68.78 | 61.2 | 113.9 | 90.24 | 78.21 |
| 107.29 | 89.97 | 79.84 | 63.29 | 92.77 | 73.24 | 64.15 |
| 90.81 | 73.28 | 65.89 | 54.26 | 119.94 | 91.43 | 78.32 |
| 112.33 | 88.4 | 76.33 | 58.67 | 102.6 | 86.77 | 78.97 |
| 93.05 | 85.33 | 81.47 | 74.04 | 144.43 | 122.7 | 113.93 |
| 122.01 | 98.43 | 88.8 | 71 | 129.06 | 113.27 | 106.24 |
| 126.69 | 97.73 | 87.11 | 72.85 | 240.59 | 98.6 | 88.27 |
| 115 | 99.14 | 92.17 | 80.65 | 117.25 | 97.58 | 87.64 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 103 | 78.71 | 67.96 | 52.85 | 103.46 | 84.72 | 74.87 |
| 160.16 | 105.73 | 98.11 | 87.45 | 117.69 | 95.41 | 84.43 |
| 109.77 | 95.53 | 87.84 | 73.58 | 83.08 | 70.75 | 63.82 |
| 117.91 | 91.06 | 82.99 | 69.8 | 137.66 | 100.35 | 90.08 |
| 101.37 | 81.18 | 71.52 | 56.93 | 152.57 | 105.2 | 92.03 |
| 83.12 | 67.95 | 61.8 | 51.45 | 107.44 | 92.89 | 84.69 |
| 117.53 | 99.88 | 91.98 | 78.84 | 109.47 | 90.83 | 81.18 |
| 98.97 | 82.41 | 75.73 | 63.9 | 106.78 | 95.25 | 89.45 |
| 61.24 | 54.79 | 50.49 | 45.49 | 105.32 | 92.08 | 84.65 |
| 86.83 | 69.55 | 62.64 | 51.4 | 118.23 | 94.57 | 84.41 |
| 102.67 | 85.09 | 77.54 | 65.42 | 89.34 | 63.79 | 52.3 |
| 112.76 | 95.68 | 88.28 | 74.34 | 98.07 | 67.29 | 54.72 |
| 89.04 | 70.02 | 62.4 | 49.9 | 97.16 | 71.07 | 58.62 |
| 103.06 | 92.3 | 87.05 | 77.37 | 103.41 | 82.19 | 71.67 |
| 97.11 | 79.94 | 71.33 | 56.48 | 103.75 | 81.95 | 71.69 |
| 82.95 | 70.31 | 63.84 | 52.96 | 99.83 | 83.19 | 74.18 |
| 115.58 | 100.57 | 92.52 | 81.54 | 142.82 | 112.09 | 100.6 |
| 113.48 | 97.87 | 89.85 | 75.06 | 162.43 | 113.28 | 102.48 |
| 73.69 | 63.36 | 58.41 | 50.31 | 86.4 | 63.29 | 53.52 |
| 71.66 | 63.53 | 58.88 | 50.81 | 96.81 | 73.45 | 63.24 |
| 165.49 | 91.09 | 74.65 | 58.66 | 97.43 | 71.56 | 58.76 |
| 120.43 | 90.45 | 80.21 | 65.7 | 102.19 | 80.87 | 68.92 |
| 113.66 | 102.97 | 96.62 | 83.93 | 115.98 | 86.94 | 71.32 |
| 76.33 | 61.28 | 55.92 | 47.84 | 106.48 | 91.66 | 84.85 |
| 89.14 | 68.56 | 61.73 | 50.64 | 118.79 | 98.44 | 88.85 |
| 103.53 | 92.85 | 87.74 | 77.48 | 111.66 | 85.93 | 74.3 |
| 157.07 | 119.05 | 102.54 | 77.8 | 154.61 | 121.76 | 103.02 |
| 94.6 | 80.96 | 75.64 | 66.92 | 125.47 | 102.43 | 93.3 |
| 115.67 | 95.26 | 84.36 | 64.79 | 115.83 | 98.78 | 89.81 |
| 87.86 | 77.58 | 72.32 | 63.28 | 124.21 | 108.75 | 99.79 |
| 108.33 | 87.29 | 79.06 | 65.51 | 102.13 | 71.87 | 58.06 |
| 84.52 | 74.4 | 68.93 | 59.28 | 109.61 | 85.97 | 74.48 |
| 104.03 | 92.69 | 87.95 | 79.01 | 94.76 | 77.3 | 69.03 |
| 95.31 | 82.36 | 76.77 | 67.31 | 112.28 | 92.88 | 81.95 |
| 134.71 | 89 | 79.08 | 63.66 | 109.77 | 92.24 | 82.01 |
| 133.03 | 97.05 | 82.57 | 61.38 | 120.8 | 102.09 | 91.3 |
| 138.03 | 121.32 | 102.72 | 79.8 | 120.54 | 99.34 | 88.46 |
| 47.83 | 39.77 | 34.87 | 19.4 | 53 | 27.87 | 25.67 |
| 57.91 | 43.04 | 37.95 | 30.97 | 81.66 | 60.48 | 53.1 |
| 98 | 88.04 | 83.51 | 73.89 | 138.2 | 111.94 | 98.17 |
| 87.12 | 75.41 | 69.4 | 59.43 | 111.41 | 85.28 | 73.42 |
| 115.58 | 100.57 | 92.52 | 81.54 | 142.82 | 112.09 | 100.6 |
| 113.48 | 97.87 | 89.85 | 75.06 | 162.43 | 113.28 | 102.48 |
| 78.13 | 66.41 | 61.91 | 53.65 | 107.69 | 89.32 | 79.81 |
| 77.31 | 64.09 | 57.81 | 47.09 | 97.51 | 77.85 | 66.55 |
| 118.26 | 100.83 | 94.07 | 81.91 | 117.98 | 87.18 | 74.67 |
| 107.96 | 90.75 | 82.9 | 68.22 | 102.95 | 83.89 | 74.23 |
| 103.53 | 91.85 | 86.74 | 76.48 | 110.66 | 84.93 | 73.3 |
| 156.07 | 118.05 | 101.54 | 76.8 | 153.61 | 120.76 | 102.02 |

| 2D_Rectum_5cc | 2D_Sigmoid_0.1cc | 2D_Sigmoid_1cc | 2D_Sigmoid_2cc | 2D_Sigmoid_5cc | 2D_Bowel_0.1cc | 2D_Bowel_1cc |
|---|---|---|---|---|---|---|
| Continous | Continous | Continous | Continous | Continous | Continous | Continous |
| | | | | | | |
| 88.37 | 32.64 | 27.74 | 25.5 | 21.21 | 25.28 | 20.99 |
| 76.19 | 86.49 | 63.17 | 54.58 | 41.01 | 101.77 | 82.88 |
| 89.89 | 35.48 | 28.95 | 25.73 | 20.21 | 26.92 | 23.49 |
| 58.73 | 15.62 | 12.06 | 11.16 | 9.16 | 16.44 | 13.2 |
| 58.25 | 23.84 | 20.32 | 19.03 | 16.67 | 19.17 | 15.7 |
| 71.6 | 48.58 | 38.34 | 34.47 | 28.91 | 15.74 | 12.33 |
| 73.23 | 38.27 | 32.18 | 29.73 | 25.9 | 17.84 | 14.52 |
| 65.7 | 31.87 | 27 | 24.19 | 18.28 | 15.16 | 11.69 |
| 76.72 | 13.7 | 10.21 | 9.4 | 7.9 | 12.17 | 9.11 |
| 82.25 | 36.63 | 32.18 | 29.98 | 25.62 | 38.8 | 31.87 |
| 75.5 | 90.95 | 67.92 | 58.84 | 45.37 | 109.03 | 97.86 |
| 63.32 | 27.99 | 23.95 | 22.22 | 19.14 | 20.33 | 17.17 |
| 59.97 | 51.91 | 40.9 | 36.2 | 29.33 | 82.19 | 63.72 |
| 80.58 | 17.72 | 14.38 | 13.25 | 11.16 | 15.03 | 11.6 |
| 65.7 | 31.87 | 27 | 24.19 | 18.28 | 15.16 | 11.69 |
| 56.92 | 23.51 | 19.78 | 18.51 | 16.38 | 61.99 | 50.83 |
| 61.6 | 38.68 | 32.97 | 30.24 | 25.56 | 80.24 | 64.44 |
| 69.32 | 33.78 | 24.85 | 21.92 | 18.3 | 33.58 | 29.2 |
| 61.35 | 23.5 | 19.58 | 17.81 | 14.73 | 33.67 | 29.51 |
| 74.46 | 41.36 | 33.98 | 30.43 | 24.48 | 69.72 | 55.34 |
| 60.55 | 13.93 | 10.82 | 9.62 | 7.68 | 21.14 | 17.67 |
| 51.54 | 30.41 | 23.84 | 20.37 | 15.07 | 53.4 | 43.69 |
| 47.55 | 17.83 | 14.08 | 12.64 | 9.16 | 13.8 | 10.42 |
| 52.01 | 33.67 | 27.21 | 24.33 | 19.87 | 21.26 | 17.73 |
| 65.31 | 50.84 | 38.96 | 34.47 | 28.03 | 29.41 | 25.1 |
| 45.41 | 35.13 | 29.28 | 26.62 | 21.97 | 37.98 | 33.04 |
| 42.04 | 17.52 | 13.94 | 13.18 | 11.56 | 21.47 | 17.89 |
| 39.88 | 10.92 | 7.37 | 6.47 | 5.16 | 11.76 | 8.53 |
| 35.81 | 9.6 | 6 | 5.33 | 3.76 | 15.04 | 11.6 |
| 33.84 | 9.33 | 5.83 | 5 | 3.52 | 14.17 | 10.94 |
| 73.77 | 25.64 | 20.88 | 18.76 | 15.29 | 14.76 | 10.28 |
| 72.82 | 19.81 | 16.27 | 14.97 | 12.48 | 25.19 | 21.01 |
| 63.52 | 17.78 | 14.46 | 13.4 | 11.46 | 28.43 | 24.2 |
| 79.77 | 31.53 | 26.85 | 24.55 | 20.68 | 71.44 | 56.55 |
| 80.08 | 40.45 | 34.53 | 31.89 | 27.47 | 60.28 | 47.87 |
| 59.32 | 18.1 | 14.98 | 13.63 | 11.37 | 15.5 | 11.9 |
| 45.82 | 20.48 | 16.84 | 15.43 | 13.33 | 38.11 | 32.48 |
| 57.32 | 19.5 | 15.58 | 14.56 | 12.24 | 23.08 | 19.62 |
| 63.45 | 21.54 | 17.37 | 15.45 | 12.22 | 38.38 | 33.07 |
| 97.52 | 34.38 | 28.8 | 26.03 | 20.11 | 15.5 | 11.93 |
| 92.49 | 33.44 | 28.03 | 25.68 | 21.55 | 78.95 | 65.7 |
| 69.51 | 19.21 | 15.58 | 14 | 11.43 | 16.71 | 13.45 |
| 69.54 | 37.25 | 28.93 | 25.59 | 20.26 | 37.26 | 23.81 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 57.59 | 40.52 | 32.69 | 29.79 | 25.52 | 80.81 | 67.73 |
| 65.83 | 21.65 | 17.49 | 15.73 | 12.92 | 17.37 | 13.84 |
| 51.5 | 19.92 | 16.13 | 14.85 | 12.76 | 105.61 | 88.12 |
| 73.32 | 20.46 | 17.18 | 15.86 | 14.06 | 15.36 | 11.05 |
| 73.97 | 25.37 | 21.51 | 19.91 | 17.53 | 40.95 | 31.86 |
| 69.96 | 23.86 | 20.63 | 19.44 | 17.44 | 53.36 | 45.17 |
| 66.38 | 13.75 | 10.27 | 8.93 | 5.43 | 15.25 | 11.71 |
| 77.75 | 19.43 | 15.59 | 13.9 | 10.41 | 21.58 | 17.94 |
| 69.66 | 14.01 | 10.99 | 9.83 | 8.57 | 15.49 | 11.92 |
| 66.25 | 15.34 | 11.84 | 11 | 9.53 | 25.27 | 21.68 |
| 35.81 | 13.4 | 9.88 | 9.09 | 7.68 | 13.17 | 9.73 |
| 36.94 | 29.79 | 24.67 | 22.43 | 19.1 | 61.77 | 52.13 |
| 40.13 | 25.98 | 21.08 | 18.9 | 15.58 | 79.7 | 57.8 |
| 54.1 | 72.21 | 52.77 | 46.27 | 38.34 | 15.41 | 11.8 |
| 55.8 | 32.51 | 27.43 | 25.21 | 21.61 | 49.74 | 43.68 |
| 58.27 | 15.44 | 11.9 | 11.13 | 9.7 | 26.99 | 23.03 |
| 83.24 | 21.83 | 18.22 | 16.88 | 14.31 | 13.57 | 9.98 |
| 86.18 | 24.44 | 20.08 | 18.13 | 14.81 | 90.45 | 63.75 |
| 38.69 | 17.72 | 14.27 | 13.47 | 11.89 | 15.38 | 11.86 |
| 47.57 | 21.52 | 17.93 | 17.02 | 15.15 | 14.79 | 11.47 |
| 39.48 | 9.65 | 6.1 | 5.38 | 3.86 | 6.96 | 3.59 |
| 48.5 | 34.51 | 27.5 | 24.88 | 20.56 | 87.42 | 64.95 |
| 45.29 | 21.23 | 17.56 | 16.07 | 13.88 | 16.94 | 13.59 |
| 71.34 | 17.82 | 14.27 | 13.1 | 11.02 | 29.27 | 25.26 |
| 72.36 | 20.61 | 17.29 | 15.93 | 14.07 | 21.03 | 17.9 |
| 53.6 | 81.38 | 58.97 | 49.2 | 35.56 | 17.05 | 13.63 |
| 73.27 | 67.5 | 50.3 | 45.13 | 36.65 | 114.76 | 97.08 |
| 76.79 | 15.99 | 12.96 | 11.78 | 10.29 | 17.52 | 13.9 |
| 73.54 | 20.14 | 16.84 | 15.57 | 13.7 | 73.1 | 62.71 |
| 82.08 | 18.6 | 15.33 | 13.98 | 12.4 | 95.55 | 78.85 |
| 38.57 | 13.42 | 9.89 | 9.12 | 7.7 | 13.86 | 10.48 |
| 55.77 | 18.25 | 15.15 | 13.87 | 12.21 | 19.16 | 15.72 |
| 56.33 | 43.69 | 37.41 | 33.73 | 26.89 | 34.61 | 29.16 |
| 63.46 | 63.43 | 51.36 | 45.72 | 37.31 | 49.79 | 40.17 |
| 64.27 | 16.92 | 13.44 | 12 | 9.81 | 13.72 | 10.37 |
| 72.54 | 48.14 | 36.25 | 32.1 | 26.74 | 101.9 | 87.85 |
| 68.84 | 18.74 | 15.2 | 13.69 | 11.15 | 14.07 | 11.04 |
| 22.09 | 9.99 | 6.98 | 5.82 | 4.56 | 13.21 | 9.77 |
| 42.2 | 13.11 | 9.7 | 8.71 | 7.45 | 17.45 | 13.92 |
| 75.25 | 17.15 | 13.67 | 12.57 | 10.07 | 13.28 | 9.8 |
| 52.74 | 54.24 | 40.36 | 35.71 | 29.09 | 42.53 | 34.09 |
| 83.24 | 21.83 | 18.22 | 16.88 | 14.31 | 13.57 | 9.98 |
| 86.18 | 24.44 | 20.08 | 18.13 | 14.81 | 90.45 | 63.75 |
| 63.92 | 11.29 | 7.8 | 6.94 | 5.32 | 20.43 | 17.06 |
| 48.43 | 11.47 | 7.92 | 7.16 | 5.35 | 51.59 | 40.15 |
| 55.63 | 17.08 | 13.63 | 12.52 | 10.92 | 37.41 | 33.01 |
| 57.3 | 17.49 | 13.9 | 12.97 | 11.1 | 95.06 | 86.08 |
| 52.6 | 80.38 | 57.97 | 48.2 | 34.56 | 16.05 | 12.63 |
| 72.29 | 66.5 | 50.21 | 44.13 | 35.65 | 113.76 | 96.08 |

| 2D_Bowel_ 2cc | 2D_Bowel_ 5cc | 3D | 3D_CTVsurface D90 | 3D_CTVsurface_ D95 | 3D_CTVsurface_ V100 | 3D_CTVsurface_ V150 |
|---|---|---|---|---|---|---|
| Continous | Continous | | Continous | Continous | Continous | Continous |
| | | | | | | |
| 19.1 | 15.82 | | 154.13 | 141.75 | 98.75 | 96.73 |
| 73.32 | 61.63 | | 158.14 | 144.68 | 99.95 | 93.47 |
| 22.19 | 20.27 | | 140 | 131 | 99.98 | 84.04 |
| 11.92 | 10.59 | | 143.38 | 133.59 | 100.04 | 86.31 |
| 14.64 | 13.13 | | 140.71 | 131.53 | 99.91 | 83.46 |
| 11.5 | 9.94 | | 135.83 | 127.87 | 99.96 | 79.46 |
| 13.59 | 11.99 | | 147.04 | 137.27 | 99.79 | 88.08 |
| 10.71 | 9.44 | | 155 | 145.36 | 100 | 92.75 |
| 7.8 | 6.4 | | 143.56 | 132.6 | 98.6 | 95.6 |
| 29.4 | 25.17 | | 152.24 | 142.94 | 99.95 | 91.32 |
| 88.6 | 74.18 | | 147.11 | 139.49 | 100 | 87.95 |
| 15.9 | 14.59 | | 135.58 | 126.69 | 100 | 79.92 |
| 57.76 | 48.89 | | 147.23 | 138.19 | 100 | 88.34 |
| 10.53 | 9.33 | | 133.05 | 124.27 | 99.91 | 77.93 |
| 10.71 | 9.44 | | 155 | 145.36 | 100 | 92.75 |
| 45.95 | 37.77 | | 138.48 | 131.14 | 100 | 80.97 |
| 58.05 | 47.72 | | 139.31 | 128.43 | 99.63 | 84.13 |
| 27.27 | 23.96 | | 137.74 | 126.5 | 99.09 | 82.82 |
| 27.68 | 24.8 | | 143.53 | 134.67 | 100.02 | 85.52 |
| 49.08 | 40.5 | | 129.03 | 118.71 | 99.54 | 95.54 |
| 16.47 | 14.62 | | 132.87 | 123.95 | 99.92 | 79.03 |
| 39.28 | 32.71 | | 146.15 | 138.17 | 100.03 | 87.19 |
| 9.54 | 7.96 | | 153.67 | 136.15 | 99.8 | 91.23 |
| 16.78 | 15.25 | | 153.94 | 140.23 | 100.03 | 91.49 |
| 23.22 | 20.16 | | 134.48 | 124.99 | 99.68 | 79.14 |
| 30.83 | 26.95 | | 143.22 | 128.68 | 99.76 | 85.68 |
| 16.98 | 15.28 | | 150.62 | 135.67 | 99.76 | 90.28 |
| 7.6 | 6 | | 149.84 | 133.56 | 99.68 | 89.94 |
| 10.53 | 9.33 | | 146.92 | 135.46 | 99.96 | 88.2 |
| 9.79 | 8.47 | | 145.8 | 135.16 | 99.58 | 88.15 |
| 11.48 | 9.18 | | 132.51 | 121.79 | 98.78 | 79.45 |
| 19.37 | 16.95 | | 126.43 | 138.51 | 99.71 | 83.71 |
| 22.58 | 19.82 | | 140.94 | 126.41 | 98.86 | 84.8 |
| 49.86 | 39.67 | | 153.37 | 142.7 | 99.9 | 90.09 |
| 42.64 | 35.49 | | 136.76 | 127.55 | 100 | 81.43 |
| 11.14 | 9.67 | | 144.79 | 133.57 | 99.56 | 86.58 |
| 30.27 | 26.76 | | 141.54 | 128.76 | 99.34 | 85.77 |
| 18.42 | 10.76 | | 148.29 | 136.21 | 99.89 | 89.08 |
| 30.49 | 26.57 | | 139.29 | 129.15 | 99.72 | 84.17 |
| 11.07 | 9.41 | | 132 | 122 | 98.89 | 77.15 |
| 58.47 | 48.75 | | 138.28 | 121.17 | 99.67 | 72.88 |
| 12.24 | 10.93 | | 151.78 | 141.4 | 100.03 | 90.89 |
| 19.53 | 15.7 | | 143.84 | 132.66 | 99.29 | 86.27 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 62.73 | 53.72 | | 144.74 | 135.42 | 99.86 | 86.47 |
| 13.01 | 11.63 | | 133.81 | 124.36 | 99.7 | 79.62 |
| 75.68 | 58.76 | | 145.36 | 132.48 | 99.6 | 87.97 |
| 11.04 | 9.65 | | 155.56 | 141.81 | 99.71 | 92.57 |
| 28.65 | 24.29 | | 147 | 136.3 | 100.04 | 88.38 |
| 40.49 | 33.24 | | 144.09 | 125.23 | 99.19 | 87.14 |
| 10.74 | 9.45 | | 147.72 | 139.6 | 99.82 | 81.82 |
| 17.09 | 15.37 | | 140.92 | 131.26 | 100.02 | 88.85 |
| 11.18 | 9.74 | | 136.14 | 126.42 | 100.05 | 82.6 |
| 20.31 | 18.03 | | 134.9 | 125.94 | 99.95 | 81.44 |
| 8.8 | 7.5 | | 148.25 | 137.04 | 100.05 | 89.07 |
| 47.1 | 39.12 | | 147.11 | 136.87 | 100.01 | 88.38 |
| 50.37 | 40.08 | | 148.8 | 138.36 | 99.66 | 83.78 |
| 10.91 | 9.57 | | 136.98 | 128.41 | 100 | 80.98 |
| 40.2 | 34.34 | | 135.01 | 124.9 | 99.86 | 81.8 |
| 21.34 | 18.69 | | 133.19 | 123.66 | 100.03 | 80.93 |
| 9.29 | 7.81 | | 137.09 | 128.32 | 93.36 | 88.74 |
| 55.31 | 45.18 | | 144.54 | 131.21 | 99.92 | 85.01 |
| 11.05 | 9.63 | | 156.42 | 143.73 | 99.76 | 92.74 |
| 10.27 | 9.17 | | 152.56 | 140.61 | 99.7 | 91.23 |
| 2.52 | 1.21 | | 148.74 | 137.94 | 100.03 | 89.37 |
| 56.05 | 44.17 | | 134.12 | 122.22 | 100.02 | 82.12 |
| 12.52 | 11.33 | | 154.18 | 141.49 | 99.95 | 91.89 |
| 23.58 | 20.87 | | 148.34 | 138.84 | 99.88 | 88.97 |
| 16.77 | 14.81 | | 147.22 | 137.22 | 99.87 | 88.31 |
| 12.6 | 11.37 | | 138.2 | 128.22 | 99.71 | 83.04 |
| 88.58 | 74.7 | | 139.15 | 132.8 | 98.8 | 81.9 |
| 13.13 | 11.7 | | 139.89 | 131.95 | 100 | 83.01 |
| 57.05 | 48.62 | | 139.22 | 125.44 | 97.97 | 87.06 |
| 67.46 | 53.33 | | 139.46 | 129.87 | 100 | 83.41 |
| 9.56 | 7.97 | | 145.17 | 132.91 | 99.68 | 87.31 |
| 14.76 | 13.25 | | 146.85 | 135.64 | 100.03 | 86.42 |
| 29.76 | 23.06 | | 145.64 | 139.4 | 99.43 | 88.03 |
| 35.63 | 29.97 | | 147.41 | 140.81 | 99.98 | 84.88 |
| 9.52 | 7.95 | | 153.95 | 144.09 | 99.5 | 92.27 |
| 74 | 55.72 | | 134.55 | 121.82 | 98.4 | 80.16 |
| 9.85 | 8.63 | | 142.17 | 134.93 | 99.78 | 83.8 |
| 8.87 | 7.55 | | 151.21 | 141.28 | 99.36 | 90.82 |
| 13.17 | 11.73 | | 154.2 | 144.6 | 97.6 | 84.66 |
| 8.93 | 7.58 | | 147.61 | 134.84 | 98.82 | 83.31 |
| 30.49 | 23.13 | | 147.51 | 148.27 | 99.85 | 82.44 |
| 9.29 | 7.81 | | 137.09 | 128.32 | 93.36 | 88.74 |
| 55.31 | 45.18 | | 144.54 | 131.21 | 99.92 | 85.01 |
| 15.7 | 13.79 | | 139.4 | 128.68 | 99.9 | 84.76 |
| 37.35 | 33.1 | | 135.53 | 122.98 | 99.87 | 83.35 |
| 30.95 | 27.38 | | 136.89 | 122.21 | 99.01 | 82.66 |
| 76.57 | 60.73 | | 144.45 | 133.52 | 99.91 | 86.95 |
| 11.6 | 10.37 | | 139.2 | 129.22 | 100.02 | 83.04 |
| 87.85 | 73.7 | | 140 | 131.2 | 99.98 | 84.04 |

| 3D_CTV0.5_D90 | 3D_CTV0.5_D95 | 3D_CTV0.5_V100 | 3D_CTV0.5_V150 | 3D_Bladder_0.1cc | 3D_Bladder_1cc | 3D_Bladder_2cc | 3D_Bladder_5cc |
|---|---|---|---|---|---|---|---|
| Continous | Continous | Continous | Continous | Continous | Continous | Continous | Continous |
| | | | | | | | |
| 101.12 | 93.39 | 86.75 | 62.55 | 122.94 | 87.97 | 81.15 | 71.19 |
| 94.32 | 88.03 | 84.61 | 49.19 | 77.31 | 68.47 | 64.12 | 55.84 |
| 93.3 | 87.2 | 75.17 | 43.34 | 137.66 | 95 | 86.8 | 73.89 |
| 94.1 | 85.3 | 85.95 | 50.26 | 116.42 | 95.63 | 89.07 | 76.45 |
| 99.81 | 94.1 | 89.81 | 50.34 | 90.62 | 77.98 | 72.76 | 64.31 |
| 90.27 | 84.82 | 79.96 | 44.53 | 151.72 | 113.41 | 101.3 | 86.73 |
| 102.52 | 94.96 | 91.93 | 53.07 | 89.47 | 80.26 | 75.71 | 67.18 |
| 96.89 | 87 | 86.19 | 52.14 | 89.85 | 80.86 | 75.8 | 66.8 |
| 97.4 | 93.7 | 91.33 | 52.72 | 47.75 | 35.79 | 32.16 | 27.48 |
| 92.02 | 85.58 | 85.34 | 47.13 | 132.71 | 86.6 | 76.22 | 62.95 |
| 95.98 | 91.43 | 85.21 | 46.38 | 90.66 | 77.27 | 69.66 | 40.21 |
| 92.38 | 85.7 | 82.83 | 46.54 | 103.13 | 91.35 | 85.39 | 74.92 |
| 97.65 | 91.44 | 87.88 | 51.02 | 81.53 | 73.92 | 70.05 | 61.76 |
| 93.91 | 87.88 | 83.41 | 46.71 | 99.77 | 82.27 | 75.43 | 63.98 |
| 96.89 | 87 | 86.19 | 52.14 | 89.85 | 80.86 | 75.8 | 66.8 |
| 94.19 | 88.57 | 83.41 | 44.53 | 99.05 | 85.68 | 78.55 | 66.05 |
| 95.44 | 86.86 | 86.09 | 51 | 115.99 | 85.45 | 72.6 | 55.25 |
| 96.49 | 88.02 | 87.29 | 51.14 | 116.42 | 89.55 | 80.23 | 67.18 |
| 95.58 | 88.51 | 85.81 | 48 | 62.59 | 52.98 | 48.16 | 40.37 |
| 93.7 | 83.71 | 84.47 | 48.7 | 72.15 | 59.2 | 52.26 | 42.02 |
| 94.81 | 89.46 | 84.47 | 48.16 | 91.57 | 73.33 | 66.54 | 54.07 |
| 100.15 | 93.32 | 90.16 | 51.31 | 100.81 | 79.29 | 69.7 | 53.95 |
| 96.36 | 88.07 | 87.15 | 50.86 | 100.71 | 85.53 | 79.81 | 69.99 |
| 96.01 | 86.85 | 87.62 | 53.57 | 117.8 | 96.53 | 87.39 | 61.28 |
| 97.88 | 90.92 | 88.11 | 50.14 | 85.44 | 76.81 | 72.06 | 62.91 |
| 98.01 | 90 | 88.38 | 50.1 | 98.12 | 80.92 | 72.73 | 58.91 |
| 102.74 | 95.18 | 92.26 | 53.37 | 71.8 | 57.58 | 51.94 | 43.38 |
| 99.72 | 90.39 | 89.81 | 53.23 | 29.96 | 24.88 | 22.63 | 19.21 |
| 94.8 | 87.52 | 85.31 | 48.76 | 50.75 | 37.55 | 32.79 | 25.38 |
| 95.71 | 88.36 | 85.74 | 48.17 | 27.2 | 23.21 | 21.44 | 18.56 |
| 95.32 | 85.21 | 87.01 | 50.39 | 92.6 | 76.91 | 70.87 | 61.07 |
| 99.81 | 92.21 | 89.25 | 51.62 | 89.43 | 73.08 | 65.03 | 51.46 |
| 98.51 | 91.1 | 88.67 | 50.81 | 77.55 | 52.96 | 60.48 | 41.63 |
| 104.26 | 98.41 | 93.78 | 55.31 | 92.68 | 80.2 | 73.6 | 62.16 |
| 96.86 | 90.04 | 87.49 | 51.43 | 85.91 | 71.78 | 65.7 | 55.49 |
| 98.31 | 89.39 | 88.71 | 49.21 | 73.72 | 65.16 | 61.43 | 59.69 |
| 96.77 | 88.23 | 87.74 | 51.9 | 99.96 | 83.36 | 73.94 | 43.93 |
| 101.71 | 94.47 | 91.36 | 53.94 | 78.73 | 60.37 | 54.49 | 45.49 |
| 101.65 | 94.43 | 91.33 | 53.83 | 87.68 | 69.4 | 61.03 | 47.95 |
| 90.88 | 83.41 | 81.17 | 44.7 | 79.54 | 71.68 | 68.03 | 61.24 |
| 94.25 | 88.39 | 83.61 | 44.37 | 89.43 | 73.62 | 66.51 | 53.3 |
| 97.11 | 91.08 | 87.11 | 49.66 | 87.71 | 74.83 | 69.15 | 59.3 |
| 101.13 | 91.06 | 90.73 | 53.03 | 105.4 | 89.23 | 83 | 72.31 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 95.62 | 88.95 | 86.85 | 48.12 | 95.11 | 71.79 | 61.95 | 47.94 |
| 97.74 | 89.29 | 88.43 | 52.77 | 113.49 | 82.99 | 77.77 | 69.75 |
| 105.27 | 97.46 | 93.58 | 55.87 | 92.62 | 80.69 | 74.81 | 63.81 |
| 102.51 | 95.14 | 91.99 | 54.86 | 87.24 | 74.97 | 69.97 | 60.35 |
| 101.76 | 94.13 | 91.29 | 54.24 | 89.09 | 68.99 | 60.9 | 49.23 |
| 99.8 | 90.86 | 89.86 | 52.18 | 83.89 | 67.82 | 61.44 | 50.44 |
| 97.91 | 90.79 | 88.17 | 50.41 | 107.62 | 87.62 | 78.24 | 66.98 |
| 97.22 | 90.54 | 87.7 | 51.53 | 97.47 | 73.96 | 66.62 | 56.83 |
| 95.39 | 89.53 | 85.61 | 48.58 | 51.02 | 45.6 | 43.05 | 38.39 |
| 96.78 | 91.1 | 86.99 | 49.31 | 63.55 | 53.57 | 49.63 | 40.1 |
| 98.7 | 90.65 | 89.08 | 52.29 | 90.01 | 70.19 | 63.59 | 54.48 |
| 98.9 | 92.42 | 89.02 | 50.94 | 95.48 | 80.29 | 74.35 | 63.32 |
| 96.46 | 90.62 | 86.02 | 47.64 | 77.57 | 63.6 | 56.71 | 45.34 |
| 96.01 | 89.69 | 86.08 | 47.96 | 87.74 | 78.61 | 74.2 | 66.44 |
| 92.71 | 86.44 | 83.42 | 46.65 | 83.85 | 69.11 | 61.71 | 48.95 |
| 93.42 | 87.2 | 83.55 | 45.95 | 73.52 | 60.61 | 55.08 | 45.67 |
| 95.83 | 88.21 | 86.42 | 49.61 | 92.94 | 81.47 | 75.59 | 67.21 |
| 100.85 | 94.83 | 90.81 | 51.92 | 102.31 | 89.48 | 81.93 | 74.25 |
| 99.95 | 91.97 | 89.96 | 50.78 | 67.45 | 57.83 | 53.32 | 45.94 |
| 100.95 | 93.93 | 90.87 | 50.95 | 65.59 | 58.47 | 54.4 | 47.2 |
| 99.43 | 92.96 | 89.45 | 50.96 | 105.9 | 71.45 | 61.81 | 49.94 |
| 93.84 | 87.87 | 83.52 | 45.28 | 91.71 | 70.3 | 62.99 | 52.2 |
| 100.34 | 90 | 90.18 | 55.01 | 101.01 | 91.17 | 85.29 | 74.04 |
| 96.89 | 90.77 | 86.88 | 47.4 | 61.6 | 49.95 | 45.89 | 39.55 |
| 96.87 | 91.31 | 86.7 | 48.3 | 73.99 | 57.57 | 51.87 | 42.56 |
| 96.79 | 86.56 | 87.82 | 52.27 | 83.39 | 75.24 | 71.24 | 62.93 |
| 90.2 | 87.3 | 85.8 | 49.6 | 97.55 | 75.94 | 66.76 | 52.05 |
| 95.43 | 89.2 | 85.74 | 48.87 | 87.69 | 73.61 | 68.16 | 59.87 |
| 96.4 | 89.36 | 86.77 | 51.65 | 88.97 | 72.4 | 63.64 | 48.34 |
| 90.08 | 82.96 | 81.67 | 47.07 | 72.24 | 63.52 | 59.11 | 51.79 |
| 97.41 | 89.61 | 88.05 | 53.44 | 85.04 | 71.82 | 66.39 | 55.56 |
| 99.81 | 92.22 | 89.86 | 52.34 | 69.89 | 61.25 | 57.18 | 49.64 |
| 95.53 | 90.37 | 86.52 | 49.33 | 97.23 | 85.85 | 81.07 | 72.47 |
| 97.56 | 89.45 | 88.3 | 52.56 | 84.77 | 75.98 | 71.64 | 63.18 |
| 96.05 | 90.18 | 86.1 | 48.7 | 106.36 | 78.2 | 69.79 | 56.64 |
| 96.61 | 89.15 | 87.78 | 50.82 | 92.19 | 71.03 | 60.78 | 45.32 |
| 90.06 | 85.24 | 78.27 | 42.31 | 110.9 | 80.3 | 70.96 | 56.98 |
| 100.48 | 92.49 | 90.39 | 52.38 | 26.12 | 22.62 | 21.08 | 18.59 |
| 100.04 | 90.01 | 90.02 | 53.98 | 55.15 | 41.4 | 36.78 | 30.06 |
| 95.49 | 88.29 | 85.79 | 48.24 | 83.84 | 76.19 | 72.14 | 63.54 |
| 93.86 | 86.89 | 84.52 | 47.77 | 76.16 | 65.76 | 60.69 | 52.31 |
| 95.83 | 88.21 | 86.42 | 49.61 | 92.94 | 81.47 | 75.59 | 67.21 |
| 100.85 | 94.83 | 90.81 | 51.92 | 102.31 | 89.48 | 81.93 | 74.25 |
| 97.07 | 90.61 | 87.44 | 50.48 | 67.43 | 56.14 | 52.3 | 45.43 |
| 94.08 | 86.17 | 85.56 | 49.53 | 57.94 | 49.71 | 45.49 | 38.42 |
| 95.97 | 86.18 | 86.88 | 50.54 | 107.23 | 88.89 | 82.78 | 71.95 |
| 98.24 | 90.71 | 88.58 | 51.94 | 95.51 | 80.17 | 73.37 | 60.65 |
| 95.79 | 85.56 | 87.82 | 52.27 | 84.39 | 76.24 | 72.24 | 63.93 |
| 90.5 | 88.74 | 84.05 | 53.94 | 98.55 | 76.94 | 67.76 | 53.05 |

| 3D_Rectum_ 0.1cc | 3D_Rectum_ 1cc | 3D_Rectum_ 2cc | 3D_Rectum_ 5cc | 3D_Sigmoid_ 0.1cc | 3D_Sigmoid_ 1cc | 3D_Sigmoid_ 2cc |
|---|---|---|---|---|---|---|
| Continous | Continous | Continous | Continous | Continous | Continous | Continous |
| | | | | | | |
| 102.31 | 85.87 | 79.81 | 69.14 | 23.9 | 20.08 | 18.52 |
| 99.25 | 81.91 | 73.14 | 58.54 | 72.15 | 52.1 | 44.86 |
| 106.98 | 91.53 | 84.43 | 71.72 | 27.86 | 22.8 | 20.29 |
| 99.79 | 81.61 | 71.73 | 53.9 | 13.96 | 10.9 | 9.7 |
| 92.49 | 76.74 | 68.1 | 53.59 | 19.99 | 16.92 | 15.66 |
| 100.7 | 83.65 | 75.06 | 60.95 | 43.99 | 34.45 | 30.85 |
| 94.1 | 81.32 | 74.62 | 61.97 | 29.66 | 25.3 | 23.51 |
| 87.38 | 69.51 | 62.39 | 49.43 | 21.92 | 18.24 | 16.49 |
| 99.73 | 77.88 | 68.89 | 55.17 | 10.92 | 7.57 | 6.48 |
| 97.43 | 83.58 | 27.06 | 65.26 | 28.17 | 24.57 | 22.87 |
| 98.67 | 87.37 | 81.22 | 69.51 | 70.97 | 54.24 | 47.44 |
| 93.16 | 78.37 | 70.45 | 56.97 | 21.82 | 18.31 | 17.06 |
| 99.86 | 79.32 | 70.03 | 55.39 | 39.98 | 32.42 | 29.11 |
| 98.46 | 84.46 | 78.42 | 66.23 | 15.32 | 11.81 | 10.95 |
| 87.38 | 69.51 | 62.39 | 49.43 | 21.92 | 18.24 | 16.49 |
| 90.25 | 72.66 | 65.17 | 52.65 | 19.81 | 16.51 | 15.44 |
| 97.51 | 74.4 | 66.02 | 50.88 | 31.3 | 26.58 | 24.47 |
| 96.61 | 83.75 | 75 | 58.68 | 28.41 | 21.1 | 18.72 |
| 86.88 | 71.35 | 84.36 | 52.44 | 20.31 | 16.86 | 14.33 |
| 102.46 | 82.75 | 74.65 | 60.14 | 33.5 | 27.54 | 24.66 |
| 92.05 | 73.48 | 63.92 | 48.69 | 11.98 | 8.96 | 7.75 |
| 96.77 | 78.95 | 68.76 | 47.56 | 27.88 | 21.93 | 18.85 |
| 105.4 | 74.23 | 62.5 | 46.79 | 16.26 | 12.82 | 11.33 |
| 91.96 | 72.86 | 63.5 | 48.67 | 28.04 | 23.07 | 20.84 |
| 99.77 | 80.93 | 71.92 | 56.56 | 48.26 | 36.58 | 32.15 |
| 94.19 | 71.18 | 59.37 | 42.89 | 31.32 | 26.09 | 23.87 |
| 84.14 | 65.29 | 55.26 | 38.13 | 16.16 | 13.09 | 11.87 |
| 71.04 | 52.71 | 45.82 | 36.99 | 10.51 | 7.31 | 5.99 |
| 57.45 | 45.73 | 39.78 | 30.47 | 9.11 | 5.69 | 4.71 |
| 49.91 | 41.94 | 38 | 31.15 | 9.07 | 5.67 | 4.67 |
| 112.21 | 89.69 | 77.56 | 57.27 | 17.98 | 14.53 | 13.12 |
| 109.91 | 87.66 | 76.24 | 56.62 | 17.35 | 13.77 | 12.56 |
| 98.81 | 78.89 | 68.66 | 52.74 | 15.81 | 12.51 | 11.48 |
| 100.28 | 85.03 | 76.77 | 62.18 | 23.19 | 19.46 | 17.84 |
| 94.31 | 79.32 | 72.44 | 59.83 | 29.69 | 25.32 | 23.48 |
| 98.5 | 80.25 | 70.14 | 53.2 | 16.77 | 13.4 | 12.07 |
| 89.4 | 69.36 | 60.36 | 42.7 | 19.87 | 16.32 | 14.88 |
| 89.69 | 71.9 | 61.98 | 45.27 | 16.86 | 13.47 | 12.17 |
| 103.79 | 83.91 | 75.98 | 60.15 | 18.6 | 14.97 | 13.38 |
| 115.52 | 101.02 | 93.85 | 80.3 | 31.42 | 25.76 | 23.16 |
| 98.74 | 88.23 | 82.83 | 71.98 | 26.18 | 21.96 | 20.11 |
| 107.96 | 85.63 | 76.82 | 60.32 | 16.51 | 13.22 | 11.83 |
| 101.63 | 85.01 | 76.35 | 60.44 | 29.6 | 23.25 | 20.69 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 91.3 | 74.27 | 65.51 | 50.3 | 33.84 | 27.13 | 24.54 |
| 98.25 | 80.76 | 71.38 | 55.77 | 18.04 | 14.52 | 13.09 |
| 92.76 | 77.42 | 69.23 | 54.83 | 29.12 | 25.34 | 23.84 |
| 110 | 90.38 | 81.51 | 66 | 17.87 | 14.66 | 13.62 |
| 100.8 | 81.83 | 73.69 | 59.01 | 20.88 | 17.48 | 16.17 |
| 109.67 | 93.3 | 84.27 | 68.83 | 22.09 | 19.05 | 17.78 |
| 95.86 | 79.5 | 70.9 | 57.71 | 11.97 | 8.88 | 7.51 |
| 104.63 | 89.07 | 82.07 | 70.55 | 16.63 | 13.17 | 11.67 |
| 89.1 | 77.65 | 71.3 | 58.86 | 13.33 | 9.84 | 9.01 |
| 88.14 | 74.79 | 67.28 | 53.69 | 13.84 | 10.6 | 9.63 |
| 75.56 | 54.71 | 45.14 | 31.25 | 12.64 | 9.4 | 8.13 |
| 79.39 | 55.3 | 45.4 | 31.96 | 25.24 | 20.86 | 19.07 |
| 79.5 | 59.26 | 49.26 | 34.32 | 22.52 | 17.95 | 16.13 |
| 90.18 | 72.31 | 63.29 | 48.43 | 65.69 | 47.4 | 41.31 |
| 93.28 | 73.52 | 64.2 | 49.35 | 27.41 | 23.09 | 21.25 |
| 83.68 | 70.59 | 63.33 | 50.05 | 14.35 | 11.2 | 9.94 |
| 105.26 | 87.94 | 80.49 | 67.81 | 17.97 | 14.82 | 13.54 |
| 100.31 | 83.8 | 77.02 | 68.45 | 18.16 | 14.89 | 13.5 |
| 77.25 | 56.87 | 48.14 | 34.91 | 16.85 | 13.51 | 12.35 |
| 91.35 | 67.91 | 58.63 | 44.18 | 20.25 | 17.13 | 15.84 |
| 85.94 | 63.14 | 51.79 | 34.69 | 9.19 | 5.74 | 4.81 |
| 79.66 | 63.41 | 54.35 | 38.52 | 26.88 | 21.49 | 19.44 |
| 102.46 | 77.03 | 63.31 | 40.21 | 19.17 | 15.62 | 14.31 |
| 95.9 | 80.93 | 74.52 | 62.17 | 15.64 | 12.08 | 11.17 |
| 103.03 | 83.76 | 75.68 | 61.68 | 17.94 | 14.83 | 13.66 |
| 91.08 | 69.71 | 60.2 | 43.33 | 48.72 | 37.63 | 33.61 |
| 95.76 | 77.36 | 66.32 | 48.24 | 62.48 | 46.03 | 38.83 |
| 101.73 | 86.59 | 79.36 | 65.83 | 15.25 | 11.78 | 10.9 |
| 87.47 | 73.49 | 66.3 | 53.96 | 18.66 | 13.34 | 11.99 |
| 103.91 | 91.38 | 83.76 | 68.87 | 15.87 | 12.68 | 11.63 |
| 75.92 | 54.69 | 44.91 | 30.35 | 12.52 | 9.33 | 8 |
| 75.41 | 60.53 | 52.65 | 39.44 | 15.77 | 12.41 | 11.53 |
| 89.45 | 72.17 | 64.22 | 52.14 | 35.78 | 31.01 | 28.26 |
| 112.58 | 89.19 | 77.35 | 59.9 | 41.9 | 36.11 | 33.1 |
| 103.45 | 85.8 | 76.07 | 59.94 | 15.81 | 12.49 | 11.31 |
| 103.64 | 85.09 | 75.1 | 58.42 | 31.84 | 24.84 | 22.16 |
| 94.41 | 78.94 | 70.55 | 55.97 | 15.57 | 11.97 | 10.99 |
| 31.75 | 26.81 | 24.78 | 21.42 | 9.98 | 6.94 | 5.8 |
| 73.8 | 56.53 | 50.46 | 40.72 | 12.95 | 9.59 | 8.51 |
| 114.02 | 94.05 | 83.02 | 64.44 | 15.39 | 11.85 | 10.92 |
| 100.74 | 74.82 | 63.94 | 45.24 | 40.46 | 30.55 | 27.55 |
| 105.26 | 87.94 | 80.49 | 67.81 | 17.97 | 14.82 | 13.54 |
| 100.31 | 83.8 | 77.02 | 68.45 | 18.16 | 14.89 | 13.5 |
| 92.25 | 77.97 | 70.33 | 57.18 | 10.28 | 7.17 | 5.91 |
| 91.16 | 69.71 | 59.35 | 43.23 | 10.37 | 7.22 | 5.93 |
| 100.98 | 74.87 | 64.05 | 47.78 | 15.57 | 11.97 | 11.19 |
| 91.8 | 74.38 | 65.97 | 51.31 | 17.87 | 14.64 | 13.56 |
| 91.08 | 69.71 | 60.2 | 43.33 | 62.48 | 46.03 | 38.83 |
| 95.76 | 77.36 | 66.32 | 48.24 | 48.72 | 37.63 | 32.61 |

| 3D_Sigmoid_5cc | 3D_Bowel_0.1cc | 3D_Bowel_1cc | 3D_Bowel_2cc | 3D_Bowel_5cc |
|---|---|---|---|---|
| Continous | Continous | Continous | Continous | Continous |
| | | | | |
| 15.47 | 19.98 | 16.66 | 15.28 | 12.99 |
| 33.44 | 83.72 | 67.79 | 60.57 | 50.75 |
| 15.93 | 21.99 | 18.97 | 17.76 | 16.09 |
| 7.91 | 15.7 | 12.09 | 11.37 | 9.83 |
| 13.73 | 17.25 | 13.79 | 12.89 | 11.47 |
| 25.61 | 14.95 | 11.57 | 10.46 | 9.29 |
| 20.79 | 16.85 | 13.5 | 12.33 | 11.2 |
| 12.66 | 13.5 | 9.95 | 9.23 | 7.77 |
| 5.3 | 15.41 | 11.87 | 11.07 | 9.67 |
| 19.53 | 29.6 | 24.67 | 22.55 | 19.6 |
| 37.25 | 101.7 | 84.14 | 75.85 | 63.29 |
| 14.68 | 18.09 | 14.93 | 13.78 | 12.41 |
| 23.89 | 67.14 | 52.62 | 48.06 | 41.07 |
| 9.14 | 14.29 | 11.21 | 9.94 | 8.85 |
| 12.66 | 13.5 | 9.95 | 9.23 | 7.77 |
| 13.64 | 43.84 | 37.59 | 34.59 | 29.56 |
| 20.92 | 59.38 | 48.77 | 44.23 | 37.22 |
| 15.59 | 28.25 | 24.51 | 22.92 | 20.15 |
| 12.64 | 29.39 | 25.27 | 23.65 | 21.24 |
| 19.82 | 56.52 | 44.87 | 39.7 | 32.8 |
| 6.03 | 17.86 | 14.68 | 13.61 | 11.93 |
| 13.92 | 49.12 | 40.06 | 36.08 | 30.16 |
| 8.17 | 13.59 | 9.96 | 9.24 | 7.77 |
| 17.2 | 19.39 | 15.8 | 14.92 | 13.48 |
| 25.98 | 26.71 | 22.51 | 20.82 | 17.99 |
| 19.92 | 35.3 | 30.68 | 28.71 | 25.22 |
| 10.56 | 19.77 | 16.47 | 15.51 | 13.86 |
| 4.93 | 11.49 | 7.91 | 7.14 | 5.71 |
| 3.44 | 14.46 | 11.14 | 9.9 | 8.73 |
| 3.42 | 13.9 | 10.59 | 9.62 | 8.03 |
| 10.72 | 13.78 | 8.13 | 7.39 | 5.87 |
| 10.32 | 20.96 | 17.36 | 15.88 | 13.91 |
| 9.65 | 24.58 | 20.84 | 19.31 | 16.93 |
| 15.25 | 45.13 | 37.95 | 34.38 | 28.6 |
| 20.46 | 31.84 | 24.57 | 21.52 | 17.18 |
| 10.09 | 14.71 | 11.47 | 10.28 | 9.15 |
| 12.92 | 34.3 | 29.17 | 27.17 | 23.92 |
| 10.36 | 20.28 | 17.14 | 15.88 | 14.5 |
| 11.36 | 30.35 | 26.39 | 24.7 | 21.88 |
| 17.65 | 13.91 | 10.76 | 9.68 | 8.09 |
| 16.87 | 63.02 | 51.84 | 46.07 | 38.38 |
| 9.66 | 15.48 | 11.92 | 11.17 | 9.67 |
| 16.39 | 29.9 | 19.89 | 16.7 | 13.57 |

| | | | | |
|---|---|---|---|---|
| 20.97 | 70.01 | 58.27 | 53.38 | 45.8 |
| 10.6 | 15.96 | 12.57 | 11.61 | 10.02 |
| 21.8 | 65.32 | 53.85 | 49.12 | 41.32 |
| 11.96 | 14.96 | 11.55 | 10.43 | 9.27 |
| 14.41 | 32.88 | 26.69 | 24.11 | 20.69 |
| 15.95 | 49.36 | 42.24 | 38.15 | 31.52 |
| 4.46 | 14.32 | 11.2 | 9.93 | 8.83 |
| 9.04 | 19.21 | 15.79 | 14.93 | 13.45 |
| 7.61 | 14.96 | 11.52 | 10.37 | 9.23 |
| 8.09 | 21.94 | 18.67 | 17.51 | 15.68 |
| 7.08 | 12.84 | 9.53 | 8.39 | 7.24 |
| 16.22 | 47.87 | 41 | 37.48 | 31.6 |
| 13.4 | 65.97 | 48.53 | 42.56 | 34.17 |
| 33.96 | 14.69 | 11.47 | 10.27 | 9.17 |
| 18.27 | 42.05 | 36.84 | 33.99 | 29.17 |
| 8.84 | 23.91 | 20.12 | 18.71 | 16.36 |
| 11.43 | 12.84 | 9.49 | 8.3 | 7.19 |
| 11.15 | 70.27 | 49.23 | 43.14 | 35.37 |
| 11.19 | 14.88 | 11.55 | 10.43 | 9.27 |
| 14.07 | 14.42 | 11.26 | 9.96 | 8.91 |
| 3.51 | 8 | 4.1 | 3.2 | 1.3 |
| 16.09 | 65.35 | 49.12 | 42.63 | 33.94 |
| 12.3 | 15.83 | 12.55 | 11.61 | 10.01 |
| 9.34 | 19.23 | 15.68 | 14.55 | 12.97 |
| 11.89 | 23.98 | 20.73 | 19.41 | 17.33 |
| 26.82 | 15.53 | 11.95 | 11.23 | 9.77 |
| 28.38 | 82.23 | 67 | 60.91 | 51.05 |
| 9.43 | 16.44 | 13.3 | 11.99 | 10.96 |
| 10.62 | 56.86 | 48.5 | 44.08 | 37.4 |
| 9.97 | 74.04 | 53.49 | 46.87 | 38.17 |
| 6.93 | 13.63 | 9.93 | 9.18 | 7.73 |
| 9.92 | 17.56 | 13.92 | 13.17 | 11.69 |
| 23.06 | 29.41 | 25.08 | 23.16 | 20.05 |
| 27.9 | 40.12 | 32.97 | 29.44 | 24.96 |
| 9.17 | 13.56 | 9.96 | 9.25 | 7.78 |
| 18.64 | 53.99 | 43.78 | 39.31 | 32.42 |
| 8.85 | 13.33 | 9.84 | 9.02 | 7.64 |
| 4.5 | 13.21 | 9.73 | 8.79 | 7.49 |
| 7.32 | 17.37 | 13.84 | 13 | 11.63 |
| 8.62 | 12.32 | 9.25 | 7.96 | 6.9 |
| 22.5 | 35.71 | 28.67 | 25.72 | 21.45 |
| 11.43 | 12.84 | 9.49 | 8.3 | 7.19 |
| 11.15 | 70.27 | 49.23 | 43.14 | 35.37 |
| 4.72 | 18.28 | 15.08 | 13.79 | 12.02 |
| 4.62 | 37.01 | 29.99 | 27.7 | 24.9 |
| 9.52 | 33.61 | 29.42 | 27.51 | 24.25 |
| 11.78 | 85.06 | 73.4 | 60.8 | 53.84 |
| 28.38 | 15.53 | 11.95 | 11.23 | 9.77 |
| 25.82 | 82.23 | 67 | 60.91 | 51.05 |